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Proposed Registration Decision PRD2014-16

Flutriafol

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Overview

Proposed Registration Decision for Flutriafol

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Flutriafol Technical Fungicide and Fullback 125 SC Fungicide containing the technical grade active ingredient flutriafol to control fungal diseases on apples, grapes, strawberries and soybeans.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Flutriafol Technical Fungicide and Fullback 125 SC Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

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[1] "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

[2] "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on flutriafol, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on flutriafol, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Flutriafol?

Flutriafol is a demethylase inhibitor fungicide with systemic activity. This active ingredient provides broad spectrum control of certain ascomycetes and rust fungi on a range of crops.

Health Considerations

Can Approved Uses of Flutriafol Affect Human Health?

Fullback 125 SC Fungicide, containing Flutriafol, is unlikely to affect your health when used according to label directions.

Potential exposure to flutriafol may occur through the diet (food and water) or when handling and applying the end-use product Fullback 125 SC Fungicide. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

In laboratory animals, the technical grade active ingredient flutriafol was of high acute toxicity by the oral route; consequently, the hazard signal words "DANGER – POISON" are required on the label. It was of low acute toxicity dermally and through inhalation exposure. Flutriafol was non-irritating to the skin, and did not cause an allergic skin reaction. Flutriafol was mildly irritating to the eyes; consequently, the hazard signal words "EYE IRRITANT" are required on the label.

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[3] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

The acute toxicity of the end-use product Fullback 125 SC Fungicide containing flutriafol was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and slightly irritating to the skin. Fullback 125 SC Fungicide did cause an allergic skin reaction; consequently, the hazard signal words "POTENTIAL SKIN SENSITIZER" are required on the label.

Flutriafol did not cause cancer in animals and did not damage genetic material. There was no indication that flutriafol caused damage to the nervous system or immune system. Health effects in animals given repeated doses of flutriafol included effects on the liver, red blood cells, adrenal gland, spleen and on skeletal development. In all species investigated, flutriafol affected body weight, which was also often accompanied by reduced food consumption.

When flutriafol was given to pregnant or nursing animals, effects of a serious nature (mortality, skeletal malformations) were observed in the developing fetus and juvenile animal at doses that were toxic to the mother. The risk assessment protects against the effects of flutriafol by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and drinking water are not of concern.

Refined aggregate dietary intake estimates (food plus drinking water) revealed that infants less than one year old, the subpopulation which would ingest the most flutriafol relative to body weight, are expected to be exposed to 29% of the acceptable daily intake , and females 13 to 49 years of age are expected to be exposed to16% of the acceptable daily intake. Based on these estimates, the refined chronic dietary risk from flutriafol is not of concern for all population subgroups.

Flutriafol is not carcinogenic; therefore, a cancer dietary risk assessment is not required.

Refined acute dietary (food plus drinking water) intake estimate was 82% of the acute reference dose for all infants (less than 1 year old), the highest exposed subpopulation. The refined aggregate exposure from food and drinking water is considered acceptable for females 13 to 49 years of age at 42% of the acute reference dose.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act* . Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using flutriafol on various crops are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Proposed Registration Decision document.

Occupational risks are not of concern when flutriafol is used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Fullback 125 SC Fungicide as well as field workers re-entering freshly treated fields can come in direct contact with flutriafol residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Fullback 125 SC Fungicide must wear long-sleeved shirt and long pants, chemical resistant gloves, and shoes plus socks. The label also requires that workers do not enter treated strawberry fields, soybean fields and apple orchards for 12 hours after application. In addition, the label requires that workers do not enter treated grape vineyards for 14 days after application to do cane turning and girdling; for 7 days to do tying, training and leaf pulling; and for 12 hours to do all other activities.

Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals is not a concern.

For bystanders and people who enter fields to perform pick-your-own harvesting, exposure is expected to be much less than that for workers. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Flutriafol is Introduced into the Environment?

When Fullback 125 SC Fungicide is applied on field crops, some of it finds its way into soil and water. Flutriafol is persistent in soils and has a potential for long-term accumulation and residue carry over to the following crop season. It does not transform readily in soils as it is not broken down in the presence of sunlight, by microbes or by reacting with water. No major transformation products were detected in soils in laboratory and field studies.

Flutriafol is soluble in water and moderately to highly mobile in soils. Laboratory and field studies, along with conservative water modelling estimates indicated that it has a potential to leach and contaminate the groundwater.

The potential mobility and high persistence of flutriafol suggest that leaching is the most important route of dissipation of flutriafol in the environment. Expected environmental concentrations in runoff water generated using water models also indicated that flutriafol has a potential for transport in surface runoff water from treated areas to nearby aquatic systems.

In the aquatic environment, it moves from water to sediment and is persistent there. Flutriafol does not break down readily in the aquatic environment. No major transformation products were detected in the water or sediment phases.

Flutriafol does not accumulate in organisms.

Although properties of flutriafol indicate that it has a low potential to enter the atmosphere and travel long distances in the air, flutriafol has been detected at very low concentrations in Arctic ice cores, and in surface and groundwater in Ontario and British Columbia even though flutriafol has never been registered for use in Canada. These results indicate that flutriafol could have a potential to enter the atmosphere and travel long distances in the air.

Risk Characterization: Fullback 125 SC is applied by field sprayer and airblast sprayer on field crops. There is a potential for exposure to non-target terrestrial and aquatic habitats due to spray drift or runoff from the uses of Fullback 125 SC.

An assessment of the environmental risk for uses of Fullback 125 SC identified the following concerns:

- adverse effects on non-target terrestrial plants and wildlife habitat
- risk to amphibians and freshwater invertebrates

Value Considerations

What is the Value of Fullback 125 SC Fungicide?

Fullback 125 SC Fungicide is a broad-spectrum foliar fungicide for use on apple, strawberry, soybean and grapes.

Fullback 125 SC Fungicide has demonstrated good control of powdery mildew, rust diseases, apple scab and other economically important diseases. This product can be incorporated into Integrated Pest Management programs with other chemical and cultural controls for disease and resistance management.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Fullback 125 SC Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with flutriafol on the skin or through inhalation of spray mists, anyone mixing, loading and applying Fullback 125 SC Fungicide must wear long-sleeved shirt and long pants, chemical resistant gloves, and shoes plus socks. Workers are not allowed to enter treated strawberry fields, soybean fields and apple orchards for 12 hours after application and they are not allowed to enter treated grape vineyards for 14 days after application to do cane turning and girdling; for 7 days to do tying, training and leaf pulling; or for 12 hours to do all other activities. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Flutriafol can pose a risk to non-target terrestrial plants and aquatic organisms. Label statements as well as spray buffer zones of 1 to 2 metres are required on the label to protect sensitive aquatic and terrestrial habitats.

Label statements are required on the label for Fullback 125 SC to inform users of the potential risks of leaching, persistence and carry-over of flutriafol.

Next Steps

Before making a final registration decision on flutriafol, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

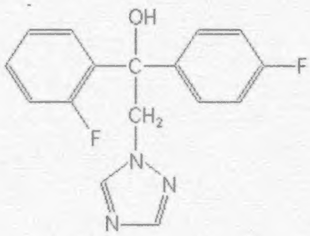
When the PMRA makes its registration decision, it will publish a Registration Decision on flutriafol (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Flutriafol

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Flutriafol
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(*RS*)-2,4′-difluoro-α-(1*H*-1,2,4-triazol-1-ylmethyl)benzhydryl alcohol
2. Chemical Abstracts Service (CAS)	α-(2-fluorophenyl)-α-(4-fluorophenyl)-1*H*-1,2,4-triazole-1-ethanol
CAS number	76674-21-0
Molecular formula	$C_{16}H_{13}F_2N_3O$
Molecular weight	301.30
Structural formula	
Purity of the active ingredient	72.6%

1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—Flutriafol Technical

Property	Result
Colour and physical state	Off-white paste
Odour	Odourless
Melting range of the pure compound	130°C
Boiling point or range	Not available

Property	Result
Density	0.99 g/cm^3
Vapour pressure of the pure compound at 20°C	4×10^{-7} Pa
Henry's law constant at 20°C	1.27×10^{-6} Pa × m^3/mole (20 ºC) 1.3×10^{-11} atm × m^3/mole (20 ºC)
Ultraviolet (UV)-visible spectrum of the pure compound	λ (nm) ε (M^{-1} cm^{-1}) 263 1490 269 1270 not expected to absorb at $\lambda > 300$ nm
Solubility of the pure compound in water at 20°C	95 mg/L
Solubility of the pure compound in organic solvents at 20°C	Solvent Solubility (g/L) Acetoner 190 Dichloromethaner 150 Hexaner 0.30 Methanol 69 Xylene 12
n-Octanol-water partition coefficient (K_{OW}) of the pure compound	Log K_{ow} = 2.3 at 20°C
Dissociation constant (pK_a)	2.3 at 25°C
Stability (temperature, metal)	Stable at 54°C for 14 days

End-Use Product—Fullback 125 SC Fungicide

Property	Result
Colour	Light beige
Odour	Weak solvents
Physical state	Liquid
Formulation type	Suspension (SU)
Guarantee	125.08 g/L
Container material and description	Plastic bottles, jugs, drums, 1L to bulk
Density	1.06 g/mL
pH of 1% dispersion in water	6.7
Oxidizing or reducing action	The product does not contain any oxidizing or reducing agents.
Storage stability	Stable for 4 years stored in HDPE containers at 20°C
Corrosion characteristics	No corrosion was observed after 4-year storage in HDPE containers at 20°C.

Property	Result
Explodability	Not explosive

1.3 Directions for Use

Fullback 125 SC Fungicide is applied preventatively to crops at early growth stages or when conditions are conducive to disease development. Application rates range between 512–1024 ml per hectare with spray intervals of 10–21 days. A shorter interval of 7–10 days is recommended prior to petal fall for apple scab control. An extended interval of 21–35 days is recommended for control of Asian soybean rust. Fullback 125 SC Fungicide must be tank mixed with Dithane DG 75 Fungicide for apple scab control and may be mixed with Headline EC Fungicide for control of asian soybean rust. A non-ionic surfactant may be added to improve control of powdery mildew on strawberry. A maximum of three to four applications may be applied per growing season depending on the crop. The maximum seasonal application rate is 2048 ml/ha for all crops.

1.4 Mode of Action

Flutriafol is a demethylase inhibitor (DMI) fungicide belonging to the triazole group (Group 3). Flutriafol disrupts sterol production in the cell walls of susceptible fungal pathogens (C14-demethylation). Group 3 fungicides are considered to have a medium risk for resistance development and can also be cross-resistant with other Group 3 active ingredients.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Flutriafol Technical have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

Gas chromatography method with mass spectrometry (GC-MS), gas chromatography with nitrogen phosphorous detection (GC-NPD) and high performance liquid chromatography with ultraviolet detection (HPLC-UV) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media.

The proposed enforcement methods utilized gas chromatography with mass spectrometry or nitrogen-phosphorus detection (GC-MS: Method RAM 219/04 or GC-NPD: ABC Study No. 49535 for plant matrices and GC-MS: Method ICIA AM00306 for animal matrices). These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices. The proposed enforcement methods were successfully validated in plant and animal matrices by an independent laboratory. Adequate extraction efficiencies were demonstrated using radiolabelled samples (rapeseed, liver) analyzed with the enforcement method.

Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for flutriafol was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of toxic effects that may result from exposure to flutriafol.

Metabolism and toxicokinetics were investigated using carbinol- and triazole-radiolabelled flutriafol in single- and repeat-dose oral studies in the rat. Characterization of the toxicokinetics of flutriafol in the blood was limited. Nevertheless, based on bile and urine excretion data, absorption appeared to be rapid and extensive. Generally 85–97% of the administered dose (AD) was absorbed within 48 h, regardless of the position of the radiolabel or dosing regime. The time at which peak concentrations occurred in the blood was not determined, and there was insufficient information to establish whether systemic exposure was dose-proportional over the range of doses investigated.

Elimination was rapid and complete (>98% of AD at 7 days). Most of the elimination in males and females occurred within 48 h (68–86% of AD); complete elimination required more time at the high dose. Approximately 50% of the administered dose was excreted in each of the feces and urine at the low dose. At the high dose there was greater elimination via the urine (61-68% of AD) than the feces (27-33% of AD). Biliary excretion at 72 h was 47 - 79% of AD; it was approximately 20% greater in males compared to females for the carbinol label. Approximately 50% of the radioactivity excreted in the bile was reabsorbed and subsequently eliminated via the urine. Slightly more radioactivity was found in the urine of animals dosed repeatedly compared to the single dosed animals. A negligible amount of label was expired as carbon dioxide. After 7 days, very little radioactivity remained in the tissues and carcass (< 3% AD), regardless of the dosing regime, dose level, or the sex of the animal.

The highest levels of radioactivity were found in whole blood, and in the liver, kidneys, adrenal glands, spleen and pituitary, regardless of the sex, dose level, or dosing regimen. In animals given low doses of flutriafol, whole blood radioactivity was 4 to 8 fold higher with repeated dosing compared to the single dose results. There was selective distribution to red blood cells. With repeated dosing, red blood cell radioactivity was 129 to 218 fold greater than corresponding plasma values. Given that more time was required for complete elimination at the high dose, systemic exposure is expected to be greater at higher doses. Characterization of organ and tissue target sites was adequate, but it was not considered particularly robust, given that these data were obtained at 7-days post-dose, well after most of the radiolabel had been eliminated.

Flutriafol was metabolized extensively and the most prevalent transformation products were structurally similar to the parent chemical. Only trace amounts of the parent were present in the urine and feces (<0.5% AD), and more than 19 metabolites were isolated. Metabolite profiles were qualitatively similar between sexes. The primary site for metabolism was the 2-fluorophenyl ring. The initial metabolic step was thought to be epoxidation followed by either rearrangement to form dihydrodiol isomers or hydroxy or dihydroxy metabolites. Subsequently, the hydroxyl groups on these primary metabolites may be either conjugated with glucuronic acid or methylated. A second, minor route for metabolism was via the removal of the triazole ring to form 1-(2 fluorophenyl)-1-(4-fluorophenyl)-ethandiol, which may then be conjugated with glucuronic acid.

In the rat, the acute oral toxicity of flutriafol ranged from slight to moderate, whereas in the mouse it was highly acutely toxic via this route. In contrast it was of low acute toxicity via the dermal and inhalation routes of exposure. Flutriafol was non-irritating to the skin in rabbits and did not cause skin sensitization in guinea pigs (Buehler and local lymph node assays). It was minimally to mildly irritating to the eyes of rabbits.

The acute toxicity of Fullback 125 SC Fungicide was low in rats via the oral, dermal and inhalation routes of exposure. In rabbits, eye irritation was minimal, while skin irritation was slight. Fullback 125 SC Fungicide caused skin sensitization in guinea pigs (Buehler assay).

Overall, in repeated dose oral toxicity studies, the liver and hematopoietic system were the main targets of flutriafol toxicity in the mouse, rat and dog. The effects on the liver, including increased weight, fatty change, hepatocellular hypertrophy, enzyme and clinical chemistry changes, were both dose and time dependent and occurred at lower doses than the hematopoietic effects that consisted of decreases in red blood cell parameters. Decreases in body weight and body weight gain were also observed in mice, rats, and dogs, with significant effects occurring in the dogs within one week of dosing via capsule. Dogs, but not rodents, were sensitive to adrenal cortical vacuolation and hemosiderin deposition in the spleen. The dog was the most sensitive species investigated, based on the body weight and liver effects.

In a 28-day dermal toxicity study in the rat, no systemic effects were observed. Skin irritation in the form of erythema and flaking occurred in females at the mid-dose and above. These effects, along with scabbing, were observed in males at the highest dose tested.

The main effects following long-term dietary exposure of flutriafol were decreases in body weight and liver toxicity, with males being slightly more sensitive than females. In both the mouse and rat long-term dietary studies, the lowest observed adverse effect levels (LOAEL) for males were lower than those for females. Effects on the liver at the LOAEL for males included a slight increase in the incidence of fatty change in mice, and slightly lower body weight and body weight gain. The difference was considered marginally adverse, and did not increase with dose. In rats, increases in the incidence of fatty change and clear cell foci were observed. The incidence of clear cell foci did not display a dose-response. Flutriafol showed no evidence of carcinogenicity in either the rat or mouse dietary oncogenicity studies.

Flutriafol was tested for potential genotoxic activity in a battery of in vitro and in vivo assays. Based on the negative results of these studies, flutriafol was not considered genotoxic.

Two dietary reproductive toxicity studies were conducted in rats, demonstrating consistent effects on parents and offspring. Reproductive and offspring toxicity occurred in the presence of parental toxicity in both studies. Parental toxicity included effects on the liver followed by decreased body weight gain at the highest dose tested. Reproductive effects in both studies included effects on the ovaries (increased weight at the highest dose tested) and reduction of the number of offspring produced. This decrease in the number of offspring was manifested as decreased litter size, pups born alive and pup mortality within one day of birth. Offspring toxicity included decreased body weight and fatty change/vacuolation in the liver at the highest dose tested.

Two gavage developmental toxicity studies were conducted in the rat. Decreased body weight gain throughout gestation was observed in the dams of both studies. In the first study, there was an increase in fetal skeletal variations (decreased ossification) down to the lowest dose tested. This effect was not observed at equivalent or lower doses in the more recent study. At higher doses in both studies, increased post-implantation loss and decreased live fetuses per dam were observed. In the more recent study, skeletal malformations (bent/misshapen/absent hyoid body, cleft palate) were also observed at the highest dose tested. In an oral capsule developmental toxicity study in the rabbit, mortality and body weight loss were observed in the dams. Increased post-implantation loss, complete litter resorptions, and skeletal variations as well as decreased fetal body weight were noted at the dose that caused significant maternal toxicity. The rabbit was the most sensitive species to the developmental effects. Results of the reproductive and developmental toxicity studies indicated that serious effects occurred in the young at doses that are toxic to the maternal animals.

There was no evidence in the acute and short-term oral neurotoxicity studies in rats that flutriafol selectively targeted the nervous system. No treatment-related gross or histopathological changes occurred in either the central or peripheral nervous system following oral exposure to flutriafol in either of these studies. In the gavage acute neurotoxicity study, at a very high dose, rats exhibited clinical signs such as dehydration, decreased motor activity, chromorhinorrhea and chromodacryorrhea. At the same high dose level there were also a number of moribund animals which exhibited a wider range of clinical signs; these animals were euthanized within two to three days of dosing. In the remaining animals, the clinical and behavioral changes at this dose level were reversible. Given the moribund condition of some of the animals, and the high dose required to elicit such effects, effects at this dose level were considered evidence of general systemic toxicity, rather than specific neurotoxicity. Consistent with the rat developmental toxicity studies, rats in the acute neurotoxicity study also exhibited acute decreases in food consumption and body weight loss. There was no evidence of neurotoxicity in the short-term oral neurotoxicity study in rats. In addition, there was very little evidence of neurotoxic potential in the broader toxicology database.

Flutriafol did not adversely impact the immune system response as measured by the IgM antibody-forming cell assay in rats in a 28-day immunotoxicity study. There was no indication in the broader toxicology database that the immune system was adversely affected by flutriafol.

Results of the toxicology studies conducted on laboratory animals with flutriafol and its associated end-use product, are summarized in Tables 2 and 3 of Appendix I. Effects seen above the LOAEL(s) have not been reported in Table 3 for most studies for reasons of brevity. The toxicology endpoints for use in the human health risk assessment are summarized in Table 4 of Appendix I.

Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA that include adverse effects to Canadian health or the environment. Incidents from Canada and the United States were searched for flutriafol, and any additional information submitted by the applicant during the review process was considered. As of 22 May 2014, no human or domestic animal incidents involving the active ingredient flutriafol have been reported to the PMRA and the applicant did not submit any additional data.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contains the standard complement of required studies as available, which included several developmental toxicity studies in rats and rabbits and two reproductive toxicity studies in rats.

With respect to potential prenatal and postnatal toxicity, no evidence of sensitivity of the young was observed in the 2-generation reproductive toxicity studies. Serious effects in the offspring (mortality up to post natal day 1) occurred at a dose level that resulted in maternal toxicity. In a developmental toxicity study in rats, skeletal malformations (hyoid, cleft palate), variations and post-implantation loss were observed in fetuses at a dose that produced decreased body weight in the mothers. In a second rat developmental toxicity study, skeletal variations were also observed in foetuses at a non-maternally toxic dose; however these effects were not considered serious. In the rabbit developmental toxicity study, post-implantation loss and decreased body weight were observed at a dose that produced mortality and bodyweight loss in the mothers.

Overall, the database is adequate for determining the sensitivity of the young and effects on the young are well-characterized. The fetal effects were considered serious endpoints although the concern was tempered by the presence of maternal toxicity. Therefore, the *Pest Control Products Act* factor was reduced to 3-fold when using the rabbit developmental toxicity study to establish the point of departure for assessing risk to women of child-bearing age. The serious effect on offspring survival occurred at or near birth, and was considered to result from in utero exposure. For exposure scenarios for children, the risk was considered well-characterized and the *Pest Control Products Act* factor was reduced to 1-fold.

3.2 Acute Reference Dose (ARfD)

Females 13-49 Years of Age

To estimate acute dietary risk (1 day), the rabbit developmental toxicity study with a no observed adverse effect level (NOAEL) of 7.5 mg/kg bw/day was selected for risk assessment. At the LOAEL of 15 mg/kg bw/day, increased post-implantation loss and intrauterine deaths were observed. It is possible these effects can result from a single exposure and are therefore relevant to an acute risk assessment. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 3-fold. **The composite assessment factor (CAF) is 300.**

The ARfD is calculated according to the following formula:

$$\text{ARfD (females 13-49 years of age)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{7.5 \text{ mg/kg bw}}{300} = 0.025 \text{ mg/kg bw of flutriafol}$$

The ARfD provides a margin of 400 to the NOAEL for malformations and fetal loss in the developmental toxicity studies in the rat.

General Population (excluding females 13-49 years of age)

To estimate acute dietary risk (1 day), the 90-day and 1-year dog studies with a NOAEL of 5 mg/kg bw/day were considered to be co-critical for risk assessment. At the LOAEL of 15 mg/kg bw/day in the 90-day study and 20 mg/kg bw/day in the 1-year study, body weight loss was observed within the first week of the study. This effect is therefore relevant to an acute risk assessment. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. **The composite assessment factor (CAF) is 100.**

The ARfD is calculated according to the following formula:

$$\text{ARfD (gen. pop)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{5\ \text{mg/kg bw/day}}{100} = 0.05\ \text{mg/kg bw of flutriafol}$$

3.3 Acceptable Daily Intake (ADI)

Females 13-49 Years of Age

To estimate risk of repeat dietary exposure, the rabbit developmental toxicity study with a NOAEL of 7.5 mg/kg bw/day was selected for risk assessment. At the LOAEL of 15 mg/kg bw/day, increased post-implantation loss and intrauterine deaths were observed. This study was considered the most appropriate in the database relevant to this population. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 3-fold. **The composite assessment factor (CAF) is 300.**

The ADI is calculated according to the following formula:

$$\text{ADI (females 13-49 years of age)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{7.5\ \text{mg/kg bw/day}}{300} = 0.025\ \text{mg/kg bw/day of flutriafol}$$

The ADI provides a margin of 400 to the NOAEL for malformations and fetal loss in the developmental toxicity studies in the rat and a margin of 460 to the NOAEL for pup mortality in the rat reproductive toxicity study.

General Population (excluding females 13-49 years of age)

To estimate risk of repeat dietary exposure, the 90-day and 1-year dog studies with a NOAEL of 5 mg/kg bw/day were considered co-critical for risk assessment. At the LOAEL of 15 mg/kg bw/day in the 90-day study and 20 mg/kg bw/day in the 1-year study, body weight loss was observed in the first week of the study. While the NOAELs in the mouse and rat long-term studies are slightly lower, the effects observed at the LOAELs were considered marginal. Also, parental rats in a two-generation reproductive toxicity study were exposed to flutriafol via the diet for an extended period to a dose between the NOAEL and LOAEL in male rats in the long-term study, and no effects on the liver or body weight were observed. Based on the nature of the effect, and the dose spacing compared to a two generation reproductive toxicity study, the effects in the long-term rodent studies were considered to be marginal and inappropriate for establishment of the ADI. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. **The composite assessment factor (CAF) is 100.**

The ADI is calculated according to the following formula:

$$\text{ADI (gen. pop)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{5\text{ mg/kg bw}}{100} = 0.05\text{ mg/kg bw/day of flutriafol}$$

Cancer Assessment

There was no evidence of carcinogenicity and, therefore, no cancer risk assessment is necessary.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Short- and Intermediate-term Dermal and Inhalation

Exposure to flutriafol is expected to be mainly via the dermal and inhalation routes for chemical handlers and through the dermal route for postapplication re-entry workers. Exposure is expected to be intermediate in duration since the product can be applied throughout the growing season (>30 days per season).

For short- and intermediate-term occupational exposures via the dermal and inhalation routes, the NOAEL of 7.5 mg/kg bw/day from the developmental toxicity study in rabbits was selected for risk assessment. At a dose of 15 mg/kg bw/day, increased post-implantation loss and intrauterine deaths were observed at a dose that produced mortality and body weight loss in the dams. Worker populations could include pregnant or lactating women and therefore these endpoints were considered appropriate for the occupational risk assessment. The available 28-day dermal study did not assess the relevant endpoints of concern (that is, effects in pups following pre-natal or post-natal exposure). A short-term inhalation study was not available; however, this study would not address the relevant endpoint of concern.

The target Margin of Exposure (MOE) for these scenarios is 300, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability as well as a factor of 3-fold for the reasons outlined in the *Pest Control Products Act* Hazard Characterization section. The selection of this study and MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

3.4.1.1 Dermal Absorption

A rat in vivo dermal absorption study was submitted. This study was reviewed and considered to be acceptable for estimating occupational exposure.

The study was well conducted and there were no major limitations. The study indicated that the skin bound residues could become available for absorption with increased time; therefore, it was deemed appropriate to use the value from the low dose group with a 10-hour exposure and 10-hour sacrifice as this value was considered to be conservative. The total amount absorbed (including skin bound residues) was 20% and this value is considered acceptable for estimating exposure to flutriafol.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to Fullback 125 SC Fungicide during mixing, loading and application. Exposure to workers mixing, loading and applying Fullback 125 SC Fungicide is expected to be intermediate in duration and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for mixer/loaders and applicators applying Fullback 125 SC Fungicide to apples and grapes via airblast and strawberries and soybeans via groundboom application equipment.

The exposure estimates are based on mixers/loaders/applicators wearing a single layer and chemical resistant gloves.

As chemical-specific data for assessing human exposures were not submitted, dermal and inhalation exposures for workers were estimated using the Pesticide Handlers Exposure Database (PHED) Version 1.1 and the Agricultural Handlers Exposure Task Force (AHETF). PHED & AHETF are compilations of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 20% dermal absorption. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight.

Dermal and inhalation exposure estimates were compared to the relevant flutriafol toxicological endpoint (no observable adverse effect level [NOAEL] = 7.5 mg/kg bw/day) to obtain the combined margins of exposure (MOEs); the target MOE is 300. The PHED and AHETF unit exposure values and estimates of exposure and risk are presented in Tables 3.4.2.1.1 and 3.4.2.1.2 Acceptable MOEs were calculated for workers who wear the proposed PPE, use the engineering controls, and follow the restrictions on the product label.

Table 3.4.2.1.1 PHED unit exposure estimates for mixer/loaders and applicators (µg/kg a.i. handled)

Scenario		Dermal	Inhalation
Mixer/loader PHED estimates			
A	All liquids, open mixing and loading (single layer plus gloves)	51.14	1.60
Applicator PHED estimates			
B	Groundboom (open cab) (single layer, no gloves)	32.48	0.96
Applicator AHETF estimates			
C	Airblast (open cab)(single layer, gloves)	3769.30	9.08
Mixer/Loader + Applicator Exposure estimates			
A+B	Open mixing/loading and open cab groundboom	84.12	2.56
A+C	(single layer, and gloves when mixing/loading)	3820.44	10.68

Table 3.4.2.1.2 Mixer/loader/applicator risk assessment for chemical handlers

Exposure scenario	Rate (kg ai/ha)	Dermal unit exposure (µg/kg a.i. handled)*	Inhalation unit exposure (µg/kg a.i. handled)*	ATPD†	Amount of ai handled per day[β]	Daily dermal exposure (µg/kg bw/day)[‡]	Daily inhalation exposure (µg/kg bw/day)[£]	Combined MOE[¶] (dermal + inhalation)
PPE: Single layer plus gloves (mixing/loading/application)								
M/L/A (farmer) Airblast	0.091	3820.44	10.68	20.0	1.82	17.38	0.24	**426**
M/L/A (farmer) Groundboom	0.128	84.12	2.56	26.0	3.33	0.70	0.11	**9301**
M/L/A (farmer) airblast	0.128	3820.44	10.68	20.0	2.56	24.45	0.34	**303**
M/L/A (farmer) Groundboom	0.128	84.12	2.56	107.0	13.70	2.88	0.44	**2260**
M/L/A (custom) Groundboom	0.128	84.12	2.56	360.0	46.08	9.69	1.47	**672**

* Unit exposure values from Table 1

† Default Area Treated per Day (ATPD) values
β Amount of ai handled per day is calculated by either multiplying the application rate by the ATPD (ha)
‡ Daily exposure = (dermal unit exposure × amount of ai handled per day × 20% dermal absorption) / (80 kg bw)
£ Daily exposure = (inhalation unit exposure × amount of ai handled per day) / (80 kg bw)
¶ Based on NOAEL = 7.5 mg/kg bw/day, target MOE = 300

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

Postapplication dermal exposure may occur when workers enter treated areas to perform various activities. The duration of exposure is considered to be short to intermediate-term as these activities may occur throughout the growing season.

Dermal exposure to workers entering treated areas is estimated by coupling dislodgeable foliar residue (DFR) values with activity-specific transfer coefficients. Chemical-specific dislodgeable foliar residue data were not submitted. As such, default DFR values of 25% of the application rate on the day of application and 10% daily dissipation were used in the exposure assessment.

The exposure estimates were compared to the flutriafol toxicological endpoint (NOAEL = 7.5 mg/kg bw/day) to obtain the MOE; the target MOE is 300. Since these values exceed the target MOE of 300 (please refer to Table 3.4.2.2.1) for strawberries, apples and soybeans, the level of postapplication exposure is not a health concern. A 12-hour restricted entry interval (REI) is adequate to protect re-entry workers for apples, strawberries, and soybeans. For grapes, additional activity specific REIs are required to mitigate exposure.

Table 3.4.2.2.1 Postapplication exposure and risk estimate for re-entering Apples, Strawberries, Grapes and Soybeans treated with Flutriafol

Crop	Activity	Rate (g ai/ha)	Predicted Peak DFR (μg/cm^2)*	Transfer coefficient (cm^2/hr)†	Dermal exposure (mg/kg bw/day)‡	MOE¶	REI◊
Apples (2 apps)	Thinning	119	0.4398	3000	0.0250	300	12 hrs
	Hand harvesting			1400	0.0123	600	
	Scouting, hand pruning, training			580	0.0051	1470	
	Hand weeding, propping, orchard maintenance			100	0.0009	8530	
Strawberries (2 apps)	Hand harvesting	128	0.4731	1100	0.0104	720	12 hrs
	Transplanting			230	0.0022	3450	
	Scouting			210	0.0020	3780	
	Hand weeding, canopy management			70	0.0007	11330	
Grapes	Turning &	1 @ 73	0.2891	19300	0.0255	300	14 days

(3 apps)	girdling	2 @ 91					
	Tying, training, leaf pulling			8500	0.0235	320	7 days
	Hand set irrigation			1750	0.0101	740	12 hrs
Soybeans (3 apps)	Scouting	2 @ 64 1 @ 128	0.3394	1100	0.0075	1000	12 hrs
	Hand weeding			70	0.0005	15780	

* Calculated using 25% dislodgeable on the day of application and 10% dissipation per day using the maximum rate and the shortest spray interval.

‡ Dermal Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/hr] × 8 hours × 20% dermal absorption) / (80 kg bw × 1000 µg/mg)

†Transfer coefficients obtained from Agricultural Reentry Task Force (ARTF) data

¶ Based on NOAEL = 7.5 mg/kg bw/day, target MOE = 300

◊ Minimum REI is 12 hours to allow residues to dry

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

Fullback 125 SC Fungicide is not a domestic product; therefore, a residential handler assessment was not required.

3.4.3.2 Postapplication Exposure and Risk

There are no residential uses for Fullback 125 SC Fungicide. However, apples and strawberries treated with Fullback 125 SC Fungicide can be harvested in pick-your-own farms. Exposure from pick-your-own harvesting is expected to be much less than that for workers and as such, a separate residential risk assessment was not required.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products and animal commodities is flutriafol. The data gathering/enforcement analytical methods are valid for the quantitation of flutriafol residues in crop and livestock matrices. The residues of flutriafol are stable in apples, cabbage, peas, rapeseed, sugar beet roots, and wheat matrices for up to 12 months; up to 5 months in soybean seed, and 2 months in soybean meal, hulls, and refined oil, when stored in a freezer at -18°C, which support the storage conditions and durations in the crop field trials and processing studies. The residues of flutriafol are stable at -20°C for 4-5 months (milk, eggs and poultry muscle and fat), and 12 months (bovine muscle, fat, liver, and kidney), which support the storage conditions and durations in the livestock feeding studies.

The raw agricultural commodities [apples, plums, peanuts, dry soybeans, grapes, and field corn] were processed, and residues of flutriafol concentrated in the following processed commodities: field corn refined oil (1.5-fold), prunes (2.2-fold), peanut refined oil (1.3-fold), soybean refined oil (1.3-fold), and sun-dried raisins (2.8-fold). Adequate feeding studies were carried out to assess the anticipated residues in livestock matrices resulting from the current uses. Crop field trials conducted throughout Canada and the United States, using end-use products containing flutriafol, at approved or exaggerated rates on crops for domestic registration (apples, grapes, strawberries, and dry soybeans), and imported commodities (bananas, sugar beets, plums, peaches, cherries, pears, field corn and peanuts) are sufficient to support the proposed maximum residue limits.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.16), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

Triazole Metabolites

Dietary exposure to 1,2,4-triazole (T), triazolyl-1-alanine (TA) and triazolyl-1-acetic acid (TAA) may occur from the use of flutriafol on food commodities. Residues of TA in plant commodities are regulated in Canada not to exceed 2.0 ppm. These metabolites are common to all triazole fungicides, including flutriafol. The cumulative risks from T, TA, and TAA will be addressed in a separate document.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the refined chronic non-cancer analysis for flutriafol: anticipated residues in processed fractions (where available), supervised trial median residue values, projected % crop treated (apples, strawberries, grapes), anticipated residues for all animal commodities, and a Level 1 estimated environmental concentration of flutriafol in potential sources of drinking water. The refined chronic dietary exposure from all supported flutriafol food uses (alone) is 0.8% (0.000194 mg/kg bw/day) of the ADI for females 13 to 49 years of age. The highest exposure and risk estimate is for children 1 to 2 years of age at 3.1% (0.001526 mg/kg bw/day). Aggregate exposure from food and drinking water is considered acceptable for all subpopulations. The PMRA estimates that the refined chronic dietary exposure to flutriafol from food and drinking water is 16.1% (0.004035) of the ADI for females 13 to 49 years of age, and 29% (0.014508 mg/kg bw/day) of the ADI in all infants (less than 1 year old), which is the highest exposure subpopulation.

3.5.2.2 Acute Dietary Exposure Results and Characterization

The following assumptions were applied in the refined acute analysis for flutriafol: 100% crop treated, anticipated residues in processed commodities, anticipated residues in animal commodities, maximum residues in non-blended and partially-blended commodities, highest average field trial (HAFT) value in blended commodities, and a Level 1 estimated environmental concentration of flutriafol in potential sources of drinking water. The refined acute dietary exposure (food alone) for all supported flutriafol food uses is estimated to be 27% (0.013562 mg/kg bw/day) of the ARfD in children 1 to 2 years of age, the highest exposed subpopulation (95th percentile, deterministic), and 7% (0.001859 mg/kg bw/day) of the acute reference dose for females 13 to 49 years of age. The refined aggregate exposure from food and drinking water is considered acceptable for females 13 to 49 years of age at 42% (0.010518 mg/kg bw/day) of the ARfD. The highest exposure and risk estimate is for all infants (less than 1 year old) at 82% (0.041148 mg/kg) of the ARfD.

3.5.3 Maximum Residue Limits

MRLs are proposed for each commodity included in the listed crop groupings in accordance with the Residue Chemistry Crop Groups webpage in the Pesticides and Pest Management section of Health Canada's website (see Table 3.5.3.1).

For additional information on Maximum Residue Limits (MRLs) in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodologies, field trial data, and acute and chronic dietary risk estimates are summarized in Tables 1, 5 and 6 in Appendix I.

Table 3.5.3.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Raisins	2.4
Stone fruits (Crop Group 12-09), small fruit vine climbing, except fuzzy kiwifruit (Crop Subgroup 13-07F), low growing berry (Crop Subgroup 13-07G)	1.5
Pome fruits (Crop Group 11-09), dry soybeans	0.4
Bananas	0.3
Peanuts	0.15
Sugar beet roots	0.08

Corn oil (refined)	0.02
Meat byproducts of cattle, goats, horses, and sheep	0.015
Eggs, fat of cattle, goats, hogs, horses, poultry, and sheep , field corn grain, meat byproducts of hogs and poultry, meat of cattle, goats, hogs, horses, poultry, and sheep, milk, popcorn grain	0.01

3.6 Exposure from Drinking Water

Estimated environmental concentrations (EECs) of flutriafol in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of flutriafol in groundwater were calculated using the PRZMGW model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PRZMGW is based on the flux or movement, of pesticide into shallow groundwater with time. EECs of flutriafol in surface water were calculated using the PRZM/EXAMS models, which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in a small vulnerable reservoir drinking water source. The parent chemical is very persistent and does not transform to any major transformation products.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EECs are expected to allow for future use expansion into other crops at this application rate. Table 3.6-1 lists the application information and main environmental fate characteristics used in the simulations. Nine initial application dates between April and July were modelled. The models were run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Table 3.6-2 below.

Table 3.6-1: Major groundwater and surface water model inputs for Level 1 assessment of flutriafol

Type of Input	Parameter	Value
Application Information	Crop(s) to be treated	apples, grapes, strawberries, and soybeans
	Maximum allowable application rate per year (g a.i./ha)	256
	Maximum rate each application (g a.i./ha)	128
	Maximum number of applications per year	2 at maximum rates
	Minimum interval between applications (days)	7
	Method of application	ground, airblast
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	stable
	Photolysis half-life in water (days)	stable
	Adsorption K_{OC} (mL/g)	163 (20th percentile of seven K_{OC} values for flutriafol)
	Aerobic soil biotransformation half-life (days)	2352 (90th percentile

Type of Input	Parameter	Value
		confidence bound on mean of nine half-life values adjusted to 25°C)
	Aerobic aquatic biotransformation half-life (days)	3029 (longest of two half-lives)
	Anaerobic aquatic biotransformation half-life (days)	2809 (only available value)

Table 3.6-2: Level 1 estimated environmental concentrations of flutriafol in potential drinking water sources (2 x128 g a.i./ha at 7-day intervals)

Compound	Groundwater EEC (μg a.i./L)		Surface Water EEC (μg a.i./L)	
			Reservoir[5]	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
Flutriafol	198	196	11.4	3.8

Notes:

1 90th percentile of daily average concentrations
2 90th percentile of yearly average concentrations
3 90th percentile of yearly peak concentrations
4 90th percentile of yearly average concentrations

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Physico-chemical properties, fate and behaviour of flutriafol in terrestrial and aquatic systems are summarized in Appendix I, Tables 7-11.

Based on its physical and chemical properties, flutriafol is considered soluble in water and has a low potential for volatilization under field conditions and from moist soil or water surfaces. It has a limited potential for phototransformation in the environment, exists as anion under environmentally relevant pH conditions and has a low potential for bioaccumulation in organisms.

Terrestrial environment: Laboratory and field studies indicated that flutriafol is persistent in soils and has a potential for long term accumulation and residue carryover to the following crop season. It is stable to hydrolysis, photolysis, aerobic and anaerobic biotransformation in soils. No major transformation products were detected in soils in any of the laboratory and field studies under Canadian field use conditions. Minor transformation products identified were 1-H-triazole and 2,4'-difluoro-benzophenone.

Based on results from batch equilibrium studies, flutriafol is expected to exhibit moderate to high mobility in soils. Based on solubility, physico-chemical properties, fate studies, mobility, water modelling and residues detected in the deeper soil layers under field conditions, flutriafol is considered as having a potential to leach and contaminate groundwater. Expected environmental concentrations in runoff water based on water models also indicated that flutriafol has a potential for transport in surface runoff water from treated areas to nearby aquatic systems.

The potential mobility and high persistence suggest that leaching is an important route of dissipation of flutriafol in the environment.

Aquatic environment: Flutriafol can enter aquatic systems through spray drift, overland runoff or through the movement of soil particles with bound residues. It is persistent in water-sediment systems under both aerobic and anaerobic conditions and is stable to hydrolysis and photolysis. Although it is persistent in water, it partitions significantly from water to the sediment. No major transformation products of flutriafol were detected in water-sediment systems. Three minor transformation products were identified in an anaerobic water-sediment study at very low concentrations: 1,2,4-triazole, 1,2,4-triazole-1-analine and 1,2,4-triazole-1- acetic acid. Mineralisation to CO_2 was low while the formation of volatile organic compounds was not significant. Based on whole fish bioconcentration factor and *n*-octonal–water coefficient (log K_{OW}) information, flutriafol is not expected to bioaccumulate in aquatic organisms.

Air: Although properties of flutriafol indicate that it has a low potential for long range atmospheric transport, it was detected in Arctic ice cores, and also at very low concentrations in surface and groundwater in Ontario and British Columbia even though flutriafol is not registered for use in Canada. Flutriafol however, does not bioaccumulate in organisms.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. The EECs are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify products and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. Screening level EECs in soil, water, aquatic eco-scenarios, vegetation and other food sources are presented in Appendix I, Tables 12-17.

A risk quotient (RQ) is calculated by dividing the exposure estimate with an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A risk assessment of flutriafol and its end-use product, Fullback 125 SC was undertaken for terrestrial organisms based on available toxicity data for earthworms (acute and chronic), bees (acute oral and contact), predatory and/or parasitic invertebrates, birds (acute oral and chronic), mammals (acute oral and chronic) and terrestrial plants (effects on seedling emergence and vegetative vigour). A summary of terrestrial toxicity data for flutriafol is presented in Appendix I, Table 16 and the accompanying screening level and refined risk assessments are presented in Tables 12 to 20.

Earthworm: The most sensitive acute LC_{50} and chronic NOEC values for earthworm in studies carried out with technical flutriafol and a formulated product were 1000 and 12.167 mg a.i./kg dry soil, respectively. The risk quotient values (EEC/ toxicity) were calculated using LC_{50} values with an uncertainty factor of 2 for the acute effects and the NOEC for the chronic effects. The EEC in soil with a cumulative rate of 256 g a.i./ha was 0.11 mg a.i./kg soil. The acute and chronic risk quotient values of less than 0.1 (Table 18) indicate that flutriafol is expected to pose a negligible risk to earthworms with the uses of Fullback 125 SC Fungicide.

Honeybee: The acute contact and oral LD_{50}s were >52.5 and 47 μg a.i./bee, respectively, with studies carried out with a relevant formulated product, and were used in the risk assessment for pollinators. The reported oral toxicity endpoint of >2 μg a.i./bee for the TGAI was not used in the risk assessment because it was considered to be overly conservative. The mortalities were less than 10% in the oral study with technical flutriafol tested with rates up to 2 μg a.i./bee. No acute contact toxicity study was provided for technical flutriafol, however, the acute contact toxicity with the end-use product is available and was used in the risk assessment. The mortalities were less than 10% in two acute contact studies tested with rates up to 52.5 μg a.i./bee.

The contact and oral exposures were estimated by multiplying the single maximum application rate of 0.128 kg a.i./ha with factors of 2.4 and 29, respectively (following the White Paper submitted to the FIFRA Scientific Advisory Panel in 2012). This procedure converts application rates (exposure) from kg a.i./ha to µg a.i./bee. The upper-bound residue value for estimating exposure to bees is based on the maximum residue value reported by Koch and Weißer (1997). The risk quotient values were calculated with the exposure estimates and LD_{50} values in µg a.i./bee and then compared with level of concern of 0.4; a risk quotient value greater than 0.4 indicates risk to bees.

The contact and oral risk quotient values of <0.006 and 0.079, respectively, (Table 18) are less than the level of concern and therefore, the uses of Fullback 125 SC Fungicide are expected to pose a negligible risk to adult bees on acute oral and contact basis.

Data to assess the risk of Fullback 125 SC Fungicide to bee larvae and adult bees on a chronic basis were not submitted. However, according to the mode of action of this chemical targeting C^{14}-demethylase in sterol biosynthesis and the low acute toxicity to adult bees, the risks for bee larvae and adults on a chronic basis resulting from the foliar spray application of Fullback 125 SC are expected to be low.

Beneficial arthropods: The screening level risk assessment was conducted using data for the two standard species, a predatory mite and a parasitoid wasp, exposed on glass plates. Risk quotients for on-field and off-field exposures were calculated. For off-field exposures, the percent drift for early and late season airblast applications and fieldsprayer applications were 74, 59 and 6%, respectively. It is noted that applying the higher drift percentages for airblast application to the cumulative application rate of 206.80 g a.i./ha for off-field calculations is a conservative approach because this rate is for the use on strawberries, for which only fieldsprayer application equipment will be used during application. Other uses of flutriafol on grapes and apples involve airblast application, but the cumulative rate of application is slightly lower. None of the on-field or off-field risk quotients exceeded the level of concern of 2 (Table 18). Therefore, the uses of Fullback 125 SC Fungicide are expected to pose a negligible risk to beneficial predators and parasites. The results of the extended laboratory studies conducted with flutriafol on various species do not indicate a potential concern.

Wild birds and mammals:

Wild birds:

Screening level assessment of risk to birds on an acute basis: The red-legged partridge was the most sensitive avian species in acute studies with a LD_{50} of 616 mg a.i./kg bw. The risk quotient values, calculated with this value and applying an uncertainty factor of 10, were less than 0.2 (Table 19), which indicate that small, medium and large birds are not at potential risk on an acute basis with the uses of Fullback 125 SC Fungicide.

Screening level assessment of reproductive risk to birds: The most sensitive species to reproductive performance is the mallard duck with a NOAEC of 39.2 mg a.i./kg diet, which equates to a NOAEL of 6.0 mg a.i./kg bw/d. The risk quotient values, calculated at the screening level by using the NOAEL (Table 19), were slightly greater than the level of concern (1.74, 1.36 and 1.41 for small, medium and large sized birds, respectively). These values indicate that the proposed uses of Fullback 125 SC Fungicide may affect the reproductive performance of small, medium and large birds and therefore the reproductive risk to birds was further characterized.

Further characterization of the reproductive risk to birds: The risk assessment for reproduction was expanded to include all relevant food guilds and food items, and also to include both on-field and off-field exposure scenarios. Because wild birds are likely to be exposed to a range of residue concentrations on food, both maximum and mean nomogram residue concentrations were considered in the assessment. To assess the risk from the consumption of food items contaminated with spray drift off the treated area, the EDE values from the screening level assessment were adjusted according to the projected percent drift that would be deposited 1 metre downwind from the site of application. A percent drift of 74, 59 and 6% was considered for early airblast, late airblast and fieldsprayer applications, respectively. It is noted that applying the higher drift percentages for airblast application to the cumulative application rate of 206.80 g a.i./ha for off-field calculations is a conservative approach because this rate is for the use on strawberries, for which only fieldsprayer application equipment will be used during application. Other uses of flutriafol on grapes and apples involve airblast application, but the cumulative rate of application is slightly lower.

Results are presented in Table 20. When considering maximum residue concentrations, on-field risk quotients slightly exceeded the level of concern, for small and medium insectivorous birds feeding on small insects (risk quotient of 1.74 and 1.36, respectively) as well as large herbivorous birds foraging on plants similar to short grass and forage crops (risk quotient of 1.41 and 1.31, respectively. With mean residues, the risk quotients did not exceed the level of concern for any of the birds feeding on the treatment area.

Off-field risk quotients slightly exceeded the level of concern only when considering maximum residues resulting from airblast early application (74% drift); risk quotients of 1.29, 1.00 and 1.05 for small and medium insectivorous birds and large herbivorous birds, respectively, as well as airblast late application (59% drift); risk quotient of 1.02 for small insectivorous birds. Risk quotients were also below the level of concern when considering exposure to mean residues for all feeding guilds both on and off the treatment area.

Based on highest risk quotient values of 1.74 (on-field) and 1.29 (off-field), it was determined that the diet of birds feeding on and off the treatment area would need to be comprised of 58% and 78%, respectively, of contaminated food items to reach the level of concern (calculated as 1/RQ × 100). It is possible that birds could consume such proportions of contaminated food items in certain situations. Birds are known to be opportunistic feeders and can sometimes feed extensively on one type of food item when it is found in abundance and when other food sources are not as readily available. However, it is noted that the above proportions are based on a diet comprised exclusively of food items contaminated with high residue levels. Given that food items are expected to contain a range of residues under field conditions (not only maximum residues), and that the level of concern is not exceeded when considering mean residues, situations where birds would experience adverse reproductive effects are less likely to occur.

The above results are based on a risk assessment carried out with the NOAEL, which is considered to be a protective endpoint given that it represents an exposure level at which no effects have been observed. To further explore the potential for reproductive concern, reproduction risk quotients were also calculated using the LOAEL, thereby providing an indication of the potential risk at an exposure level at which effects are known to occur. For this assessment, a LOAEL of 13.1 mg a.i./kg bw/d (LOAEC 97.5 mg a.i./kg diet) was used, based on reductions in hatchability (percentage of hatchlings of live 21-d embryos, percentage of hatchling of eggs set, 14-d survivors, and number of hatchlings). The risk quotients calculated with the LOAEL (Table 21) were below the level of concern for all birds feeding on food items contaminated with maximum and mean residues both on and off the treatment area. In other words, birds are not expected to be exposed to flutriafol at levels that are known to cause reproductive effects.

Overall, results suggest that the likelihood of observing reproductive effects in birds following the use of flutriafol is low given that (i) risk quotients calculated with the NOAEL and maximum residues are below the level of concern for most feeding guild / bird size combinations, and where a potential risk was identified, risk quotients do not exceed the level of concern with an important margin, (ii) risk quotients calculated with the NOAEL and mean residues are below the level of concern for all feeding guild / bird size combinations and (iii) risk quotients calculated with the LOAEL are well below the level of concern. A label statement informing the user of potential risks to birds is not warranted for flutriafol.

Wild mammals:

Screening level assessment of risk to wild mammals on an acute basis: The mouse was the most sensitive mammalian species in acute studies with an LD_{50} of 179 mg a.i./kg bw. The risk quotient values, calculated with this value and applying an uncertainty factor of 10, were 0.33, 1.05 and 0.56 for small, medium and large sized mammals, respectively (Table 22). The risk quotient value (1.05) for medium sized mammals slightly exceeded the level of concern and therefore, the acute risk to this particular group of mammals is further characterized.

Screening level assessment of reproductive risk to wild mammals: The screening level risk quotients, calculated with a NOAEL of 10.2 mg a.i./kg bw/d, were 0.59, 1.84 and 0.98 for small, medium and large sized mammals, respectively, (Table 22). These values indicate that the uses of Fullback 125 SC Fungicide may affect the reproductive performance of medium sized mammals and therefore the risk to these groups of mammals is further characterized. For small and large sized mammals, risk quotients are below the level of concern and it is not necessary to further characterize the risk.

Further characterization of risk to wild mammals: The risk assessment was expanded for medium sized mammals to include all relevant food guilds and food items and also to include both on-field and off-field exposure scenarios. For the off-field assessment, EDE values from the screening level assessment were adjusted according to the projected percent drift that would be deposited 1m downwind from the site of application (same approach as for birds; see above). Both maximum and mean nomogram residue concentrations were considered in the expanded assessment. Results are presented in Table 23.

Acute risk quotients calculated for on-field exposure to maximum residues slightly exceeded the level of concern for medium sized herbivorous mammals feeding on short grass only (risk quotient of 1.05). No concern was identified when risk quotients were calculated using on-field mean residue values or for any of the off-field scenarios. It is concluded that the acute risk to mammals with the uses of Fullback 125 SC will be negligible given that (i) the level of concern is exceeded for only one mammal size / feeding guild combination among all the possible combinations (medium mammals feeding on short grass contaminated with maximum residue values), (ii) the risk quotient for the latter case exceeds the level of concern by only a very slight margin and (iii) risk quotients calculated with mean residues are well below the level of concern for all scenarios.

Reproductive risk quotients calculated with maximum residue values exceeded the level of concern for medium sized herbivorous mammals feeding on the treatment area (highest risk quotient: 1.84) and off the treatment area following airblast applications (risk quotients of 1.26-1.36 and 1.00-1.09 for early and late airblast applications, respectively). No concern was identified for mammals feeding off the treatment area following applications with a ground boom. Also, risk quotients were below the level of concern in all cases when using mean residue values. When risk quotients are calculated using the LOAEL rather than the NOAEL (Table 24), reproductive risk quotients did not exceeded the level of concern for the medium sized mammals.

Overall, the likelihood of observing reproductive effects to mammals following the use of flutriafol is low given that (i) reproduction risk quotients calculated with the NOAECL and maximum residues exceed the level of concern by a slight margin for only one feeding guild / mammal size combination, (ii) risk quotients calculated with the NOAEL and mean residues are below the level of concern for all feeding guild / mammal size combinations and (iii) risk quotients calculated with the LOAEL are well below the level of concern. A label statement informing the user of potential risks to mammals is not warranted for flutriafol.

Terrestrial plants

Screening level risk assessment: Studies on toxicity/effects on seedling emergence and vegetative vigour indicated EC_{25} values of greater than 134 and 268 g a.i./ha (the highest applications rates tested), respectively, (Table 25). The risk quotient values were calculated using a cumulative rate of 256 g a.i./ha (assuming no dissipation between applications) for the seedling emergence and 206.80 g a.i./ha (assuming a default foliar half-life of 10 days) for vegetative vigour. The risk quotient value (<0.77) did not exceed the level of concern for vegetative vigour; however, it exceeded the level of concern (<1.91) for seedling emergence indicating that the uses of Fullback 125 SC Fungicide may adversely affect non-target terrestrial plants.

Refined risk assessment: A refined risk assessment was undertaken to characterize the risk to non-target plants due to spray drift. The maximum cumulative rate of application for strawberries was used to assess the risk to non-target plants due to spray drift for three application scenarios. The resulting cumulative rates of 189.44, 151.04 and 15.36 g a.i./ha were adjusted for the estimated percent drift for each of the application methods/timing (in other words, airblast early and late season and, ground boom, respectively; see Table 26).

The quotient values for seedling emergence for early and late airblast applications (<1.40 and <1.13, respectively) potentially exceeded the level of concern. Therefore, there is a potential risk to non-target terrestrial plants at the maximum cumulative application rate of Fullback 125 SC Fungicide. It is noted that using the maximum cumulative rate for strawberries for all three application scenarios is somewhat conservative. Risk mitigation measures, such as buffer zones are, therefore, required to protect terrestrial habitat (Table 30 and 31). The buffer zones will be calculated based on relevant crop, use patterns and application equipment.

4.2.2 Aquatic organisms

A summary of aquatic toxicity data for flutriafol is presented in Table 17. Risk to aquatic organisms was assessed using the most sensitive species in each category. The risk quotients were calculated using the appropriate uncertainty factors as described in Table 27.

Screening level

A screening level risk assessment for aquatic organisms was conducted assuming a direct overspray to water at a cumulative application rate of 255.795 g a.i./ha. Two scenarios were considered for exposure to aquatic organisms: EEC in 15 cm water depth (0.17 mg a.i./L) for exposure to amphibians and EEC in 80 cm water depth (0.032 mg a.i./L) for all other organisms including aquatic plants.

Risk quotient values greater than or equal to 1.0 indicate that the LOC is exceeded, in which case a refined risk assessment is undertaken by characterizing the contribution of spray drift and runoff separately.

Freshwater invertebrates: Risk to freshwater invertebrates was assessed using the most sensitive toxicity values of *Daphnia* sp. Acute risk was assessed using the acute LC_{50} with an uncertainty factor of 2 (0.415 mg a.i./L) and chronic risk with the chronic NOEC (0.013 mg a.i/L). The quotient value of less than one (0.07) for the acute exposure indicates that uses of Fullback 125 SC Fungicide is expected to pose negligible acute risk to freshwater inverteberates. The chronic risk quotient value (2.46), however, exceeds the LOC and, therefore, the risk will be further characterized.

Freshwater fish: Acute risk to freshwater fish was assessed using the LC_{50} value for the most sensitive species (rainbow trout, 0.92 mg a.i./L) with an uncertainty factor of 10. The chronic risk was assessed with a NOEC for the rainbow trout (0.39 mg a.i./L). The risk quotient values of less than 1 (0.35 and 0.08 for acute and chronic, respectively) indicate that the uses of Fullback 125 SC Fungicide are expected to pose a negligible risk to freshwater fish. Risk to early life-stages of fish was also assessed using a NOEC of 4.8 mg a.i./L for fathead minnow. The risk quotient value of 0.01 indicates that the uses of Fullback 125 SC are not expected to affect the early growth stage of freshwater fish.

Acute, chronic and early life-stage risk assessments indicate that the uses of Fullback 125 SC Fungicide are expected to pose a negligible risk to freshwater fish.

Amphibians: As no toxicity data on amphibians were submitted, acute risk to amphibians was assessed using the acute LC_{50} of the most sensitive fish species (rainbow trout, 0.92 mg a.i./L) with an uncertainty factor of 10. The chronic risk was assessed with a fish chronic NOEC (rainbow trout, 0.39 mg a.i./L). The EEC was estimated for a water depth of 15 cm. The risk quotient values for the acute and chronic exposures were 1.85 and 0.44, respectively. The risk quotient for acute exposure exceeds the level of concern and, therefore, acute risk to amphibians will be further characterized.

Sediment-dwelling organisms: Flutriafol is persistent in the aquatic systems and, therefore, risk to sediment-dwelling organisms was also assessed. The NOEC value for the sediment-dwelling organisms, *C. riparius,* was 1.6 mg a.i./L. The low risk quotient value of 0.02 indicates that the uses of Fullback 125 SC Fungicide are expected to pose a negligible risk to sediment-dwelling organisms.

Freshwater algae: The most sensitive freshwater algal species to flutriafol is green algae (*S. capricornutum*) with an EC_{50} of 0.57 mg a.i./L. Acute risk was assessed with an uncertainty factor of 2. The low risk quotient value of 0.11 indicates that the uses of Fullback 125 SC Fungicide are expected to pose negligible risk to freshwater algae.

Freshwater plants: The 7-d EC_{50} value for the aquatic plant, *Lemna gibba*, was 0.65 mg a.i./L. Acute risk was assessed with an uncertainty factor of 2. The risk quotient value was 0.1 and was below the level of concern, which indicates that the uses of Fullback 125 SC Fungicide are expected to pose a negligible risk to freshwater plants.

Marine invertebrates: The most sensitive marine invertebrate species is eastern oyster with an LC_{50} of 25 mg a.i./L. Acute risk was assessed with an uncertainty factor of 2. The risk quotient value was less than one (0.002), which indicates that the uses of Fullback 125 SC Fungicide are expected to pose negligible risk to marine invertebrates.

Marine fish: Acute risk to marine fish was assessed using the sheepshead LC_{50} value of >72.2 mg a.i./L) and with an uncertainty factor of 10. The risk quotient value of less than one (<0.004) indicates that marine fish are not at potential risk from the uses of Fullback 125 SC Fungicide.

Marine algae: The most sensitive marine algal species is saltwater diatom with an acute EC_{50} of 0.46 mg a.i./L. Acute risk was assessed with an uncertainty factor of 2. The risk quotient value was less than one (0.14), which indicates that the uses of Fullback 125 SC Fungicide are expected to pose negligible risk to marine algae.

Refined risk assessment: The screening level risk assessment indicated a potential chronic risk to freshwater invertebrates (risk quotient: 2.46) and acute risk to amphibians (risk quotient: 1.85). The risk was, therefore, further characterized by estimating EECs in runoff water from treated areas into a receiving water body and by considering the percentage of the spray that drifts downwind from the treated field.

Runoff:

The EECs predicted by water modelling for runoff with 50 years of continuous use of Fullback 125 SC Fungicide (Tables 13 and 14), are higher than those predicted at the screening level based on an application scenario for one season with two applications (Table 12). In general, the screening level EECs for a chemical are expected to be higher than the runoff EECs. In this case, however, some of the runoff values exceeded the direct overspray EECs. The screening level for the 80 cm deep water body is exceeded after about 20 years, and the chronic after about five years, and the acute level is exceeded after about 37 years, and is at about the maximum concentration reached in the simulation of the 80 cm water body. For the 15cm deep water body, the acute level is exceeded after about ten years, and the chronic and screening levels are not exceeded. It should be noted that the difference between the 80 cm and 15 cm results (despite the higher EECs in a 15 cm pond) are because of the endpoints used in the assessment (the chronic daphnia endpoint being more sensitive compared to the fish endpoints). It is likely that the persistence of flutriafol coupled with the lack of outflow and continual input (50 years of use) in the simulated pond result in higher run off EECs, compared to one year of applications as a direct overspray.

It should be noted that the pond eco-scenario is intended to be conservative, and in the "natural environment" there may be aquatic organisms that live in lakes and rivers whereby there is in-flow and out-flow which would result in lower expected concentrations of flutriafol.

As flutriafol is persistent in aquatic systems and the runoff EEC values were higher than screening level EECs, risk quotient values were recalculated for all the aquatic organisms using runoff EECs and the results are presented in Table 28. The risk quotient values indicated that runoff from the uses of Fullback 125 SC is expected to pose a negligible risk to *Daphnia* sp (acute), fish (acute and chronic), amphibians (chronic), freshwater midge (chronic), algae and vascular plants. The risk quotient values for runoff also did not exceed level of concern for any of the marine organisms tested, in other words, crustaceans, fish and diatom and therefore, the uses of Fullback 125 SC are expected to pose a negligible risk to these organisms.

The risk quotient values with runoff EECs, however, exceeded the level of concern for chronic effects to *Daphnia* sp (RQ: 6.85) and acute exposure to amphibians (RQ: 2.08) and, therefore, the uses of Fullback 125 SC may pose a risk to these organisms due to exposure to surface runoff water contaminated with flutriafol residues. Label statements to help reduce runoff are required on the product label for Fullback 125 SC.

Spray drift:
Three application scenarios, airblast early (74% drift) and late (59% drift), and ground boom (6% drift) were used to assess the acute risk to amphibians and the chronic risk to *Daphnia* sp due to spraydrift. The maximum application rates (two applications of 128 g a.i./ha each with 7 day interval) result in cumulative rates of 189.288, 150.919 and 15.348 g a.i./ha due to spray drift by airblast early, late and ground boom applications, respectively. The EECs in 0.15 cm water depth due to spray drift for airblast early, late and ground boom applications were 0.126, 0.100 and 0.010, respectively. The corresponding EECs in 80 cm water depth were 0.024, 0.019 and 0.002 mg a.i./L (Table 23).

The acute risk quotient values for amphibians, however, exceeded the LOC (1.37 and 1.09 for airblast early and late applications, respectively), and, therefore, the uses of Fullback 125 SC Fungicide may pose an acute risk to amphibians due to spray drift from airblast applications. The chronic risk quotient values for *Daphnia* sp with spray drift from airblast early and late applications (1.85 and 1.46, respectively) also exceeded the level of concern indicating that Fullback 125 SC Fungicide may pose a risk to freshwater invertebrates on a chronic basis. It is noted that using the maximum cumulative rate for strawberries for all three application scenarios is somewhat conservative; however, other uses of flutriafol on grapes and apples involve airblast application (in other words, greater percent drift), with cumulative rates of application slightly lower.

Conclusion: A refined risk assessment with runoff and spray drift scenarios indicated that the uses of Fullback 125 SC Fungicide may pose an acute risk to amphibians and a chronic risk to freshwater invertebrates. Risk mitigation measures such as spray buffer zones and label statements are, therefore, required to help mitigate the risk to these organisms (Table 30 and 31). Crop-specific use rates and methods of application will be used during the calculation of the spray buffer zones.

4.2.3 Incident reports

Environmental incident reports were obtained from two main sources, the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the United States Environmental Protection Agency Ecological Incident Information System (EIIS). Specific information regarding the mandatory reporting system regulations that came into force 26 April 2007 under the *Pest Control Products Act* can be found at http://www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/incident/index-eng.php.

As of 2 April, 2014, no environmental incident reports were found for flutriafol.

4.2.4 Long range transport

Low values of vapour pressure (4×10^{-7} Pa at 20 °C) and Henry's law constant (1.27×10^{-6} Pa × m^3/mole at 20°C) indicate that this compound is non-volatile under field conditions and from water/moist soil surfaces. A theoretical DT_{50} of 1.1 days based on photochemical and oxidative decomposition was reported (calculated according to the Atkinson method). Also it was reported that <3% volatilized from soil and plant surfaces in a volatilization study with labelled flutriafol formulated as a suspension concentrate. These results indicate a low potential for volatilization for flutriafol.

Flutriafol residues were, however, reported in the surface layer of an ice core dated between 1992 and 1998 and taken from the Svalbard archipelago ice cap in arctic Norway (9.8 ng/L) (Hermanson, *et al.* 2005). Water monitoring data were available for flutriafol in surface water and groundwater in Canada and in the United States. Briefly, low levels (0.00001 to 0.00413 µg/L) of flutriafol were detected in a few groundwater and surface water samples in BC and Ontario (Environment Canada's Pesticide Science Fund, PMRA 13111104, 1311110, 1311111, 1311112, 1403269, 1971119).

In the US (California and Georgia), no residues were detected in any of the surface water samples and groundwater samples were not analyzed for flutriafol (US Geological Survey National Water Quality Assessment program database, PMRA 2369634).

Given that flutriafol is not registered in Canada, the detections indicate a possible atmospheric source (atmospheric persistence and fast moving summer air masses), and the potential for this pesticide to enter the surface water as well as groundwater.

Flutriafol has, however, a low potential for bioaccumulation in organisms (log K_{OW}: 2.30 and whole fish bioconcentration factor: 7.2).

5.0 Value

5.1 Effectiveness Against Pests

Extensive provincial spray programs are implemented for apple scab control on apples and for Asian soybean rust control on soybean due to the economic and social importance of these diseases. Flutriafol has demonstrated efficacy against all of the supported diseases on these crops and provides value as an option for growers as a rotational or tank mix partner. Although there are already group 3 fungicides registered for some of the uses proposed in this submission, the registration of flutriafol provides another tool to growers and provides them with more flexibility in the implementation of spray programs. Additional options for product rotation and tank mixing allows sustainability of this product as well as other products currently registered for the supported uses.

Forty-three trials were submitted to support claims on apple. Nineteen trials conducted in the EU were considered as supplementary data. Three trials were not reviewed due to low disease pressure or application of flutriafol in tank mixes with other products registered for the same uses. Twenty-five trials (including 18 supplementary EU trials) supported the claim of control of apple scab when applied at a rate of 950 ml/ha (119 g a.i./ha) tank mixed with a protectant fungicide. The protectant fungicide to appear on the product label as the recommended tank mix partner is Dithane DG 75 Fungicide (mancozeb). An additional sixteen trials (including one supplementary trial) supported the claims of control of powdery mildew, cedar-apple rust and quince rust at rates of 585–877 ml/ha (73–110 g a.i./ha).

Four trials submitted on grape supported the claim of control of powdery mildew at 585–731 ml/ha (73–91 g a.i./ha). Six trials on strawberry supported the claim of control of powdery mildew at 585–1024 ml/ha (73–128 g a.i./ha). The use of a non-ionic surfactant on strawberry was also supported by a scientific rationale.

Twenty-two trials were submitted to support claims on soybean. One trial was considered as supplementary data as two diseases were assessed together. Two additional trials were not reviewed as the target disease did not appear. Three trials on Asian soybean rust supported the claim of control at 512–1024 ml/ha (64–128 g a.i./ha). A total of 13 trials on frogeye leafspot (9) and brown spot (4) plus one supplementary trial that assessed both diseases together supported the claims of suppression of both diseases at 512–1024 ml/ha (64–128 g a.i./ha). Three trials on cercospora leaf blight supported the claim at 512–1024 ml/ha (64–128 g a.i./ha). A tank mix with Headline EC Fungicide for resistance management of Asian soybean rust was also supported.

5.2 Economics

Apple, grape and strawberry are all commodities where revenues are dependent on fruit quality. Flutriafol has demonstrated control of major diseases on these crops, which may lead to improved yield and produce grade resulting in an economic benefit to the grower.

Asian soybean rust is a devastating disease of soybean. This disease has not been a major issue for soybean growers in Canada to date, mainly due to the diligent monitoring by growers and the use of fungicides to manage outbreaks. Due to the importance of this disease, it is important for growers to have tools like flutriafol at hand to prevent major economic losses.

5.3 Sustainability

5.3.1 Survey of Alternatives

A number of fungicides are registered on the labelled crops to control or suppress plant diseases supported for registration on the Fullback 125 SC Fungicide label. Refer to Table 33, Appendix I, for further information on alternative products.

5.3.2 Compatibility with Current Management Practices Including Integrated Pest Management

All of the labelled crops have non-conventional and/or biological fungicides registered for disease management. These products should be applied during low disease pressure events. Fullback 125 SC Fungicide has long application intervals, but non-conventional products can be applied during the interval to further reduce infection. Monitoring for inoculum or infection levels will aid in timing applications of Fullback 125 SC Fungicide and rotational products. The combination of the long interval and the integration of conventional and non-conventional products acting together may help to reduce disease pressure. Reduced disease pressure allows the use of registered rates at the lower end of the range and may reduce the number of applications per season of conventional fungicides. Cultural methods such as pruning and canopy management will allow better spray penetration as well as removing sources of secondary inoculum which will also contribute to reducing fungicide use. Although other Group 3 fungicides are registered on the labelled crops, there are sufficient alternate products from other mode of action groups to allow rotation of flutriafol into a disease management program.

5.3.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Flutriafol is a demethylation inhibitor (DMI) fungicide categorized as a Group 3 fungicide by the Fungicide Resistance Action Committee. All of the crops on the Fullback 125 SC Fungicide label have other DMI fungicides registered for most of the supported diseases. Group 3 fungicides have a medium risk of developing resistance and can also be cross-resistant with other DMI fungicides, so preparation of a spray schedule is important in managing resistance. Several of the supported pathogens are considered at high risk of developing resistance; for example, resistant isolates of *Venturia inaequalis* and *Erysiphe necator* have been noted in field populations. Both of these pathogens have multiple mode of action active ingredients registered for disease management, so integration of flutriafol into spray programs should be manageable.

General Fungicide Resistance Action Committee recommendations for the use of DMI fungicides on the labelled crops are preventative use or application at early stages of disease, application at full rates using the recommended timings and spray volumes, and alternation and tank mixing with different mode of action fungicides to reduce resistance risk. No more than four applications of DMI fungicides per season should be made, so the maximum number of seasonal applications was amended for certain crop/pest combinations to observe this recommendation.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy: in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, flutriafol and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Flutriafol does not meet Track 1 criteria, and is not considered a Track 1 substance as bioaccumulation factor (log K_{OW} 2.3) does not meet the criterion of log K_{OW}. See Table 32, Appendix I, for comparison with Track 1 criteria.

- Flutriafol does not form any transformation products that meet all Track 1 criteria.

Technical grade flutriafol and the end-use product Fullback 125 SC Fungicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

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[5] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette.*[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including DIR99-03 and DIR2006-02,[8] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- The end-use product, Fullback 125 SC Fungicide has, as a component, the preservative 1,2-benzisothiazoline-3-one, which contains low levels of polychlorinated dibenzodioxins and furans (TSMP Track 1). As the use of this preservative was recently re-evaluated and found to be acceptable, and because the input of dioxins into the environment from pesticides is being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of TSMP, the Agency position is that no further action is required.

- Cyclopentasiloxane, decamethyl (D5) at 0.1%: The Chemical Management Plan review of D5 indicates that this formulant/impurity was categorised as non-toxic as defined by the *Canadian Environmental Protection Act*. The PMRA Chemical Management Plan Working Group recategorised D5 to List 4B. As the conditions listed under 4B are met, no further assessment is required.

- Cyclotetrasiloxane, octamethyl (D4) at 0.0043%: The Chemical Management Plan screening assessment of D4 indicates that this substance is entering or may be entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biodiversity. This substance was declared "toxic" under section 64 of the *Canadian Environmental Protection Act*, 1999. The PMRA Chemical Management Plan Working Group decided to keep this chemical in List 2 category. Given that this chemical is present as an impurity at negligible amounts, no concern is expected and, therefore, no action is warranted at the present time.

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[6] *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

[7] NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

[8] DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

Although the PMRA has not yet proposed a risk management strategy for D4 in pest control products, the concentrations in the proposed product are below those in other registered pest control products.

The Government of Canada proposed risk management strategies include limiting the quantity or concentration in other consumer products manufactured in and imported into Canada. D4 is found in pest control products at similar levels to those in other consumer products.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02 .

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for flutriafol is adequate to define the majority of toxic effects that may result from exposure. There was no evidence of carcinogenicity in rats or mice after longer-term dosing. There was no evidence of increased susceptibility of the young in reproduction or developmental toxicity studies; however, serious effects (fetal loss, skeletal malformations) were observed in the presence of maternal toxicity. Flutriafol is not neurotoxic or immunotoxic. In short-term and chronic studies on laboratory animals, the primary target was the liver, hematopoietic system, adrenal gland, and spleen. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Mixer, loader and applicators handling Fullback 125 SC Fungicide and workers re-entering treated apples, strawberries, grapes and soybeans are not expected to be exposed to levels of flutriafol that will result in risks of concern when Fullback 125 SC Fungicide is used according to label directions. The personal protective equipment on the product label is adequate for protection.

The nature of the residues in plants and animals is adequately understood. The residue definition for enforcement is flutriafol in plant products and in animal matrices. The proposed use of flutriafol on the various crops does not constitute a risk of concern for chronic or acute dietary exposure (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend MRLs. The PMRA recommends that the following MRLs be specified for residues of flutriafol.

Commodity	Recommended MRL (ppm)
Raisins	2.4
Stone fruits (Crop Group 12-09), small fruit vine climbing, except fuzzy kiwifruit (Crop Subgroup 13-07F), low growing berry (Crop Subgroup 13-07G)	1.5
Pome fruits (Crop Group 11-09), dry soybeans	0.4
Bananas	0.3
Peanuts	0.15

Sugar beet roots	0.08
Corn oil (refined)	0.02
Meat byproducts of cattle, goats, horses, and sheep	0.015
Eggs, fat of cattle, goats, hogs, horses, poultry, and sheep , field corn grain, meat byproducts of hogs and poultry, meat of cattle, goats, hogs, horses, poultry, and sheep, milk, popcorn grain	0.01

7.2 Environmental Risk

Flutriafol is persistent and does not transform readily in soils and aquatic systems, and has a potential for residue carry over to the following crop season. It does not form any major transformation products. Minor transformation products detected were1-H triazole (1,2,4-triazole), 2,4'-diflurobenzophenone , 1,2,4-triazole-1-analine and 1,2,4-triazole-1-acetic acid. Flutriafol is mobile and has a potential to leach and contaminate the groundwater, and to be transported to non-target areas through surface runoff.

Flutriafol with the proposed uses of Fullback 125 SC Fungicide presents a negligible risk to soil organisms, bees, beneficial arthropods, fish, algae, aquatic plants and marine organisms. It may, however, pose a risk to non-target terrestrial plants from spray drift, and to amphibians and aquatic invertebrates due to runoff and spray drift. In order to minimize the potential risk, spray buffer zones between the treated area and downwind sensitive terrestrial and aquatic habitats, and precautionary label statements are required.

7.3 Value

The data submitted to register Fullback 125 SC Fungicide are adequate to demonstrate value and support use of this product on the supported crops and diseases.

The Canadian Grower Priority Database (CGPD) compiles and prioritizes grower-identified priorities for crop pest protection. Growers have identified the supported apple, grape and strawberry diseases plus Asian soybean rust as priorities on the database. The registration of Fullback 125 SC Fungicide will address these requests and provide growers with an additional tool for disease management on the labelled crops.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Flutriafol Technical Fungicide and Fullback 125 SC Fungicide containing the technical grade active ingredient flutriafol to control fungal diseases on apples, grapes, strawberries and soybeans.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Human Health

Because there is a concern with users coming into direct contact with flutriafol on the skin or through inhalation of spray mists, anyone mixing, loading and applying Fullback 125 SC Fungicide must wear long-sleeved shirt and long pants, chemical resistant gloves, and shoes plus socks. Workers are not allowed to enter treated strawberry fields, soybean fields and apple orchards for 12 hours after application and they are not allowed to enter treated grape vineyards for 14 days after application to do cane turning and girdling; for 7 days to do tying, training and leaf pulling; or for 12 hours to do all other activities. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Flutriafol can pose a risk to non-target terrestrial plants and aquatic organisms. Label statements as well as spray buffer zones of 1 to 2 metres are required on the label to protect sensitive aquatic and terrestrial habitats.

Label statements are required on the label for Fullback 125 SC to inform users of the potential risks of leaching, persistence and carry-over of flutriafol.

List of Abbreviations

♀	female
♂	male
µg	micrograms
1/n	exponent for the Freundlich isotherm
abs	absolute
AD	administered dose
a.i.	active ingredient
ADI	acceptable daily intake
AFC	Antibody forming cells
AHETF	Agricultural Handlers Exposure Task Force
ALS	acetolactate synthase
ALT	Alanine aminotransferase
AP	Alkaline phosphatase
APDM	Aminopyrine-N-Demethylase
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
AST	Aspartate aminotransferase
ATPD	area treated per day
atm	atmosphere
bw	body weight
bwg	bodyweight gain
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CGPD	Canadian Grower Priority Database
CL	confidence limit
cm	centimetres
DF	dry flowable
DFR	dislodgeable foliar residue
DMI	Demethylase inhibitor
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in concentration)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
ER_{25}	effective rate for 25% of the population
EU	European Union
F1	first generation
F2	second generation
fc	food consumption
fe	food efficiency
FOB	functional observation battery
g	gram

GD	gestation day
h	hour
ha	hectare(s)
hct	hematocrit
HD	high dose
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IPM	Integrated Pest Management
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LD	low dose
LD_{50}	lethal dose to 50%
LLNA	Local Lymph Node Assay
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre(s)
MAS	maximum average score for 24, 48 and 72 hours
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
M/L/A	Mixer/Loader/Applicator
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NC	Not Classified
NCE	normochromatic erythrocyte
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
P	parental generation
PBI	plantback interval
PCE	polychromatic erythrocyte

PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal day
PPE	Personal protective equipment
ppm	parts per million
RBC	red blood cell
REI	Restricted entry interval
rel	relative
RLD	repeat low dose
RSD	relative standard deviation
S9	supernatant 9 (metabolic activator agent)
SC	soluble concentrate
SER	smooth endoplasmic reticulum
SI	stimulation index
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TC	Transfer coefficient
TGAI	technical grade active ingredient
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v	volume
v/v	volume per volume dilution
WBC	white blood cell
wk	week
wt	weight

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Soil	N/A	Active	GC-MS	0.01 ppm	2115621
Sediment	Soil method can be extended for sediment.				2115621
Drinking water	N/A	Active	GC-NPD	0.05 µg/mL	2115623
Ground water	N/A	Active	GC-NPD	0.05 µg/mL	2115623
Surface water	N/A	Active	GC-NPD	0.05 µg/mL	2115623
Fresh water	N/A	Active	HPLC-UV	0.02 µg/mL	2115622
Salt water	N/A	Active	HPLC-UV	0.02 µg/mL	2115622
Plant	RAM 219/04 ABC Study No. 49535	Flutriafol	Enforcement and data gathering: Gas chromatography with nitrogen-phosphorus detector (NPD) or mass spectrometry (MS)	0.01 0.05 (soybean meal); 0.5 (aspirated grain fractions)	2115914 2115915
Animal	ICIA AM00306 (modifications dated 13-August-2007 and 8-October-2007)	Flutriafol	Enforcement and data gathering: Gas chromatography with mass spectrometry (GC-MS)	0.01 (milk, eggs, muscle, fat, liver, kidney)	2115910 2115913

Table 2 Toxicity Profile of Fullback 125 SC Fungicide Containing Flutriafol

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons.

Study Type/Animal/PMRA #	Study Results
Oral gavage Rat, Wistar-derived PMRA# 2115964	LD50 > 2000 mg/kg bw **Low toxicity**
Dermal Rat, Wistar-derived PMRA# 2115965	LD_{50} > 2000 mg/kg bw **Low toxicity**
Dermal Rat, Wistar-derived PMRA# 2115966	LD_{50} > 4000 mg/kg bw **Low toxicity**

Study Type/Animal/PMRA #	Study Results
Inhalation Rat, Sprague-Dawley PMRA# 2115967	$LC_{50} > 2.02$ mg/L **Low toxicity**
Eye Irritation Rabbit, New Zealand White PMRA# 2115968	$MAS_{24\text{-}72\,h} = 8.1/110$ (♀) **Minimally irritating**
Skin Irritation Rabbit, New Zealand White PMRA# 2115969	$MAS_{24\text{-}72\,h} = 0.7/8$ (♀) **Slightly irritating**
Skin sensitization (Buehler Method) Guinea pig PMRA# 2115971	Positive response in 20% of animals **Potential skin sensitizer**
Skin sensitization (LLNA) Mice PMRA# 2407341	SI = 3.0 at 10 % (w/v) (♀) **Potential skin sensitizer**

Table 3 Toxicity Profile of Technical Flutriafol
(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.)

Study Type/ Animal/ PMRA #	Study Results
Toxicokinetic Studies	
PMRA# 2115503, 2115504, 2115506 Rat (excreta including bile, metabolites, tissue distribution)	14C-flutriafol (carbinol and triazole labels) as single and 14-day repeated doses of 5 mg/kg bw (LD and RLD, respectively) or single doses of 250 mg/kg bw (HD) in polyethylene glycol 600; 2-5 rats/sex/dose; bile excretion assessed; euthanized at 48, 72, or 168 h post-dose or post final dose **Absorption:** Rapid and extensive. Based on bile and urine excretion data, more than 85% of AD generally appears to be absorbed within 48 h in males and females (except HD females, 38% of AD was apparently absorbed), regardless of the label and dosing regime. Although toxicokinetic parameters were not determined, it appears that the time-course of absorption was longer at the high dose. **Distribution:** Tissue-specific distribution was assessed at 7 days post-dose. The highest levels of radioactivity were found in whole blood, and in the liver, kidneys, adrenal glands, spleen and pituitary, regardless of the

Study Type/ Animal/ PMRA #	Study Results
	sex, dose level, or dosing regime. Compared to LD animals, whole blood radioactivity in RLD males and females was 8-fold and 4-fold higher, respectively. Compared to plasma, red blood cell radioactivity was 218-fold and 129-fold greater in RLD males and females, respectively. This indicates selective distribution to red blood cells. **Metabolism:** Metabolism was extensive. Only trace amounts of the parent were present in the urine and feces (<0.5% AD), and more than 19 metabolites were isolated (3 identified, 3 tentatively identified). Metabolite profiles were qualitatively similar between sexes, but there were a few modest quantitative differences among the transformation products. With few exceptions, greater amounts of identified compounds were isolated in the feces and urine of the HD group compared to the RLD group. The primary site for metabolism was the 2-fluorophenyl ring. The initial metabolic step was thought to be epoxidation followed by either rearrangement to form the dihydrodiol isomers or hydroxy or dihydroxy metabolites. The hydroxyl groups on these primary metabolites may then be either conjugated with glucuronic acid and/or methylated. A second, minor route for metabolism was via the removal of the triazole ring to form 1-(2 fluorophenyl)-1-(4-fluorophenyl)-ethandiol, which may be subsequently conjugated with glucuronic acid. **Elimination:** Elimination was rapid and complete (> 98% at 7 days). Most of the elimination occurred within 48 h (> 86% AD at LD & RLD, > 68% AD at HD), but more time was required for complete elimination at the HD. Given that more time was required for complete elimination at the HD, systemic exposure is expected to be greater at higher doses. At 72 h, excretion via the bile accounted for 47-79% AD. For the carbinol label, bile excretion was approximately 20% greater in males compared to females. Also, approximately 50% of the radioactivity excreted in the bile was reabsorbed and eliminated via the urine. Overall, approximately 50% of the AD was excreted in each of the feces and urine at the LD. At the HD there was greater elimination via the urine (61-68% AD) than the feces (27-33% AD). Similarly, slightly more radioactivity was found in the urine of animals dosed repeatedly compared to the single dosed animals. A negligible amount of label was expired as carbon dioxide (<0.05% AD). After 7 days, very little radioactivity remained in the tissues and carcass (< 3% AD), regardless of the dosing regime, dose level, or the sex of the animal.
Acute Toxicity Studies - TGAI	
Oral gavage Mouse, Alderley Park PMRA# 2115526, 2115527	LD_{50} ♂ = 365 mg/kg bw LD_{50} ♀ = 179 mg/kg bw LD_{50} ♂,♀ not reported **High acute toxicity**
Oral gavage Rat, Alderley Park PMRA# 2115526, 2115527	LD_{50} ♂ = 1140 mg/kg bw LD_{50} ♀ = 1480 mg/kg bw LD_{50} ♂,♀ > 1000 and < 1500 mg/kg bw **Slight acute toxicity**
Oral gavage Rat, Wistar PMRA# 2115525	LD_{50} ♀ > 300 and < 2000 mg/kg bw **Moderate acute toxicity**

Study Type/ Animal/ PMRA #	Study Results
Dermal Rat, Sprague-Dawley PMRA# 2115528	$LD_{50} > 2000$ mg/kg bw **Low acute toxicity**
Inhalation Rat, Sprague-Dawley CD IGS BR PMRA# 2115530	$LC_{50} > 5.20$ mg/L **Low acute toxicity**
Eye Irritation Rabbit, New Zealand White PMRA# 2115531	$MAS_{24\text{-}72\,h} = 3.3/110$, eyes rinsed at 1 h **Minimally irritating**
Eye Irritation Rabbit, New Zealand White PMRA# 2115532	$MAS_{24\text{-}72\,h} = 18.7/110$ (♀) **Mildly irritating**
Eye Irritation Rabbit, New Zealand White PMRA# 2115533	$MAS_{24\text{-}72\,h} = 13.3/110$ (♂) **Minimally irritating**
Skin Irritation Rabbit, New Zealand White PMRA# 2115535	$MAS_{24\text{-}72\,h} = 0/8$ **Non-irritating**
Skin sensitization (Buehler Method) Guinea pig PMRA# 2115536	**Negative (♂)** **Not a skin sensitizer**
Skin sensitization (LLNA) Mouse, CBA/Ca PMRA# 2115537	Negative (♀) **Not a skin sensitizer.**

Study Type/ Animal/ PMRA #	Study Results
Short-Term Toxicity Studies	
28-Day dietary Rat, Wistar PMRA# 2115543	Supplemental Mortality: One female fed 5000 ppm (Day 7) **≥ 10 mg/kg bw/day:** ↑ liver wt (♂) (*non-adverse)* **≥ 30 mg/kg bw/day:** ↑ APDM activity; hepatocyte hypertrophy (♂); ↓ MCHC (*non-adverse*) (♀) **≥ 80 mg/kg bw/day:** ↑ centrilobular hepatocellular hypertrophy (♂) (*non-adverse*) **≥ 200 mg/kg bw/day:** ↑ WBC, liver toxicity (↑ liver wt, fatty change, hydropic degeneration); ↓ bw, ↓ bwg, hematological parameters (↓ RBC, hemoglobin, MCHC; *non-adverse*), ↓ triglycerides, SER proliferation, ketosis (♂); ↓ kaolin-cephalin time, ↑ centrilobular hepatocellular hypertrophy, ↑ cholesterol (♀) **500 mg/kg bw/day:** ↓ bw, ↓ bwg, ↓ fc, ↓fe, liver toxicity (↑ centrilobular hepatocyte hypertrophy), clinical signs (stained pelt, thin body, hunched posture, piloerection, ptosis and convoluted eyelids), hematological parameters (↓ hemoglobin, hct; *non-adverse*), ↓ kaolin-cephalin time, ↑ ALT, ↑AST, ↑ Urea, ↓ triglycerides, ketosis, focal margination of macrophages; clinical signs (↑ chromolachrymation, stained snout, incontinence, hypothermia), ↓ spermatogenesis, ↑ contracted seminal vesicle tubules, ↑ prostate atrophy (♂) ; hair loss, subdued appearance (♀)
90-Day dietary Rat, Wistar PMRA# 2115538	NOAEL = 14/22 mg/kg bw/day in ♂/♀ LOAEL = 158/145 mg/kg bw/day in ♂/♀ **≥ 1.5/1.6 mg/kg bw/day:** *all non-adverse*, ↓ fc (sporadic at this dose) (♂); ↓fc (♀) **≥ 14/22 mg/kg bw/day:** *all non-adverse*, ↑ APDM activity; ↑ SER proliferation, ↑ hepatocyte vacuolation (♂); ↑ cholesterol, ↑ liver wt (♀) **158/145 mg/kg bw/day:** ↓ bw and bwg, hematological parameters (↓ hemoglobin, hct, MCHC; *non-adverse*), ↓ kaolin-cephalin time (↑ 13%, *non-adverse*), ↑ cholesterol, liver toxicity (↑ liver wt, ↑ hepatocyte vacuolation/fatty change, centrilobular hepatocyte hypertrophy, ↑ SER proliferation, ↑ APDM activity); ↓ triglycerides (♂)
90-Day oral (capsule) Dog, beagle PMRA# 2115539, 2115540	NOAEL = 5 mg/kg bw/day LOAEL = 15 mg/kg bw/day **15 mg/kg bw/day:** liver toxicity (↑ liver wt, alkaline phosphatase activity, APDM activity, ↑ hemosiderin-laden Kupffer cells); ↑ WBC (neutrophil, monocytes; *non-adverse*), ↑ spleen hemosiderin content, ↑ spleen wt (♂); bw loss (wk 1 -2), ↓ bw, bwg, ↑ triglycerides (♀)

Study Type/ Animal/ PMRA #	Study Results
12-Month oral (capsule) Dog, beagle PMRA# 2115541, 2115542	NOAEL = 5 mg/kg bw/day LOAEL = 20 mg/kg bw/day Mortality: One animal at 20 mg/kg bw/day was killed for humane reasons due to poor condition (wk 16), but was unclear whether it was treatment related (♀) **20 mg/kg bw/day:** ↓ bwg, ↑ platelets, liver toxicity (↑ liver wt, alkaline phosphatase activity, triglycerides, sinusoidal cell hemosiderin pigmentation, ↓ albumin), ↑ adrenal cortical vacuolation (zona fasciculata), ↑ adrenal wt, ↑ spleen hemosiderin pigmentation; hematological parameters (↓ hemoglobin, hct, RBC) (♂); bw loss (wk 1–2 and at wk 1-53), ↓ bw, ↑ WBC (*non-adverse* , neutrophils, lymphocytes), centrilobular hepatocyte lipid, kidney wt (*non-adverse*) (♀)
14-Day dermal Rat, Sprague Dawley Range-finding PMRA# 2115544	Supplemental **≥ 250 mg/kg bw/day:** ↑ bwg (*non-adverse*) (♀) **1000 mg/kg bw/day:** ↑ bwg (*non-adverse*), chromodacryorrhea (red tears), erythema (grade 1) (♂);↑ fc (*non-adverse*) (♀)
28-Day dermal Rat, Sprague Dawley PMRA# 2115545	**Systemic:** NOAEL = 1000 mg/kg bw/day LOAEL not established. Systemic toxicity: No adverse effects observed. **Dermal:** NOAEL = 250 mg/kg bw/day LOAEL = 500 mg/kg bw/day **≥ 500 mg/kg bw/day:** ↑ erythema and flaking (both grade 1) (♀) **1000 mg/kg bw/day:** ↑ scabs; ↑ erythema and flaking (both grade 1) (♂)
Chronic Toxicity/Oncogenicity Studies	
24-Month dietary oncogenicity Mouse PMRA# 2115452, 2115455, 2115457, 2115461, 2115463, 2115465	NOAEL: = 10/50 ppm (1.1/7.4 mg/kg bw/day ♂/♀) LOAEL = 50/200 ppm (5.9/31 mg/kg bw/day ♂/♀) **≥ 5.9/7.4 mg/kg bw/day:** ↓ bw, bwg, ↑ liver toxicity (fatty change) (♂) **24/31 mg/kg bw/day:** ↑ eye discharge, ↓ fc, ↑ liver wt, centrilobular hepatocellular hypertrophy; ↑ blood cell counts (platelet, WBC, neutrophil, lymphocytes) (♂); ↑ thickened eyelids, ↓ bw, bwg , ↑ liver toxicity (fatty change) (♀) **No evidence of oncogenicity.**

Study Type/ Animal/ PMRA #	Study Results
24-Month dietary toxicity/oncogenicity Rat, Wistar-derived PMRA# 2115446, 2115450, 2115451, 2401110	NOAEL = 20/200 ppm (1.02/12.2 mg/kg bw/day, ♂/♀) LOAEL = 200/2000 ppm (10.0/122 mg/kg bw/day, ♂/♀) **≥ 10/12.2 mg/kg bw/day:** ↑ kidney wt (*non-adverse*); ↑ liver wt, fatty change, small discoloured foci (gross), clear cell altered hepatic foci (♂) **102/122 mg/kg bw/day:** Clinical signs (↑ thin animals, ↓ distended abdomens), ↓ bw, ↓ bwg, ↓ fc, ↓ fe (early, transient), hematological parameters (*all non-adverse* ↓ hemoglobin, hct, MCV, MCH), liver toxicity (↑ liver wt, enlargement, discoloured foci, centrilobular hypertrophy,↑ Fatty change; ↓ triglycerides, ↓ AP, ↑ ALT, severe liver necrosis (1 animal) (♂);↑ cholesterol, total protein, liver toxicity (bile duct proliferation/cholangiofibrosis, hemosiderin accumulation in Kupffer cells (♀) **No evidence of oncogenicity.**
Developmental/Reproductive Toxicity Studies	
2-Generation dietary reproductive toxicity Rat, Wistar-derived PMRA# 2115467, 2115468, 2115474	Parental toxicity: NOAEL: 60/240 ppm (4.8/21.9 mg/kg bw/day, ♂/♀) LOAEL: 240/1000 ppm (20.6/103 mg/kg bw/day, ♂/♀) **≥ 20.6/21.9 mg/kg bw/day:** ↑ liver wt (P rel. & F_1 abs.) ↑ fatty change in liver (F_1) (♂) **88.7/103 mg/kg bw/day:** ↓ bwg (P & F1 premating), fc (P premating), ↑ liver wt (P & F_1), ↑ fatty change in liver (P); ↑ centrilobular hepatocellular hypertrophy (P & F_1) (♂); ↓ bw (P gestation), bwg (P & F_1 gestation), fc (F_1 premating), fe (F_1 premating), ↑ fatty change in liver (F_1) (♀) Reproductive toxicity: NOAEL: 1000/240 ppm (88.7/21.9 mg/kg bw/day, ♂/♀) LOAEL: not established/1000 ppm (not established/103 mg/kg bw/day, ♂/♀) **88.7/103 mg/kg bw/day:** ↑ ovary weight, ↓ litter size (F_2, decrease PND 1), percent of pups born live (F_2), proportion of litters with all pups born live (F_2) (♀) Offspring toxicity: NOAEL: 240 ppm (21.9 mg/kg bw/day, ♀) LOAEL: 1000 ppm (103 mg/kg bw/day, ♀) **88.7/103 mg/kg bw/day:** ↓ bwg (F_{1a}), ↑ fatty change in liver/ fine vacuolation of hepatocytes (F_{1b} & F_{2b}) **No evidence of sensitivity of the young** **Serious effect in the young (mortality)**

Study Type/ Animal/ PMRA #	Study Results
2-Generation dietary reproductive toxicity (range-finding) Rat, Wistar PMRA# 2115476, 2115477	Supplemental Parental toxicity: **≥ 17.3/19.1 mg/kg bw/day:** ↑ hepatocellular hypertrophy, liver fatty change (diffuse/centrilobular); ↓ bwg (gestation) (♀) **72/81 mg/kg bw/day:** ↑ liver wt (assessed in control & HD groups only); ↑ ruffled fur (1 dam on day 22 & 23, total litter loss on day 24 following parturition), ↓ bw, bwg (PND 1-14), ↓ fc, ↑ enlarged liver (♀) Reproductive toxicity: **≥17.3/19.1 mg/kg bw/day:** ↑ post-implantation loss (♀) **72/81 mg/kg bw/day:** ↑ testes wt, epididymal wt (♂); ↓ implantation sites, ↑ stromal cell hyperplasia in ovaries, ↓ gestation index, ↓ birth index (♀),↑ pups born dead pups, ↓ mean number of live pups per litter at delivery, ↑ early post natal loss, Offspring toxicity: **81 mg/kg bw/day:** ↓ viability index (PND 4, 16% decrease), ↑ total pup loss, ↓ mean number of living pups on day 21, ↓ bw & bwg (lactation, rearing), ↓ fc (wk 1 of rearing); delayed vaginal opening/sexual maturation (♀) **No evidence of sensitivity of the young.** **Serious effect in the young (mortality).**
2-Generation dietary reproductive toxicity Rat, Wistar PMRA# 2115478, 2115479	Parental toxicity: NOAEL: 150 ppm (10.2/11.6 mg/kg bw/day, ♂/♀) LOAEL: 300 ppm (20.8/23.9 mg/kg bw/day, ♂/♀) **20.8/23.9 mg/kg bw/day:** ↑ fatty change (P, F1 ♂); ↑ liver wt (P), hepatocellular hypertrophy (♂) Reproductive toxicity: NOAEL: 300/150 ppm (20.8/11.6 mg/kg bw/day, ♂/♀) LOAEL: Not established/300 ppm (not established/23.9 mg/kg bw/day, ♂/♀) **20.8/23.9 mg/kg bw/day:** ↑ pup mortality [F1; PND0-1] Offspring toxicity: NOAEL: 150 ppm (11.6 mg/kg bw/day, ♀) LOAEL: 300 ppm (23.9 mg/kg bw/day, ♀) **23.9 mg/kg bw/day**: ↑ pup mortality [F1; PND0-1] **No evidence of sensitivity of the young.** **Serious effect in the young (mortality)**

Study Type/ Animal/ PMRA #	Study Results
Developmental toxicity, oral gavage Rat, Wistar PMRA # 2115480, 2115482, 2405768, 2405769, 2405770	Maternal toxicity: NOAEL: 50 mg/kg bw/day LOAEL: 125 mg/kg bw/day **125 mg/kg bw/day:** ↑ staining of the genital/ventral fur (primarily during dosing period, 7, 8, 4, 16 dams, resp), ↓ bwg (GD 6-15, GD 15-21; GD 0-21, uncorrected and corrected for mean gravid uterine wt), fc Developmental toxicity: NOAEL: not determined LOAEL: 10 mg/kg bw/day **≥ 10 mg/kg bw/day:** ↑ skeletal variations (not ossified calcaneum/calcanea: bilateral, unilateral or bilateral; partially ossified occipital; not ossified odontoid), *manus* and *pes* scores (decreased ossification) **Evidence of sensitivity of the young** **Serious effect in the young (mortality) at 125 mg/kg bw/day**
Developmental toxicity, oral gavage, range-finding Rat, Wistar PMRA # 2115483	Supplementary Maternal toxicity: **≥ 50 mg/kg bw/day:** ↑ clinical signs (pushing head through bedding, transient), ↓ bwg, fc **150 mg/kg bw/day:** ↑ mortality (1 dam euthanized *in extremis* on GD 12, bw loss from GD 8), clinical signs (2 dams, transiently ruffled fur and hunched posture; 1 dam, vaginal bleeding, day 14; both dams had complete litter resorptions), ↓ bw Developmental toxicity: **50 mg/kg bw/day:** ↑ skeletal variations (rudimentary cervical ribs, rudimentary supernumerary thoracic ribs, zygomatic arch fusion, ong cervical ribs, cervical rib fused to thoracic rib cartilage, branched xiphoid cartilage, ↓ non-ossification of proximal phalanges of toe #5) **150 mg/kg bw/day:** ↑ total litter resorptions, post-implantation loss, early resorptions, ↓ live fetuses (3 delivered, one abnormal: domed head, ablepharia, micrognathia, and assumed cleft palate), ↓ fetal bw **No evidence of sensitivity of the young** **Serious effect in the young (mortality, malformations)**
Developmental toxicity, oral gavage, range-finding Rat, Wistar PMRA # 2115484	Supplementary Maternal toxicity: **100 mg/kg bw/day:** ↓ bw (day 20-21), bwg (GD 6-9), fc Developmental toxicity: **100 mg/kg bw/day:** ↑ post-implantation loss, early resorptions, late resorptions, ↓ fetal bw, ↑ skeletal malformations (palatines reduced with cleft palate, hyoid body absent, interrupted, bent), ↑ skeletal variations

Study Type/ Animal/ PMRA #	Study Results
	(maxilla and mandible, blue-stained area(s) and/or focus(i); squamosal or post-tympanic process, additional ossification; squamosal blue focus(i); zygomatic arch fusion; hyoid body, accentuated curvature; long cervical ribs; rudimentary cervical ribs; pelvic girdle, caudal displacement; supraoccipital cartilage with hole; additional ventral plate; cervical rib cartilage fused with thoracic rib 1 cartilage; costal cartilage joins sternum asymmetrically; supernumerary thoraco-lumbar costal cartilage detached from the vertebral column), ↑ skeletal variations (supernumerary full ribs; supernumerary rudimentary ribs; non-ossified proximal phalanges of digit #5; non-ossified left talus; non-ossified proximal phalanges of toe #2, 3, and 4; interrupted costal cartilage #11; supernumerary costal cartilage #1, left; long costal cartilage, left) **No evidence of sensitivity of the young** **Serious effect in the young (mortality, malformations)**
Developmental toxicity, oral gavage Rat, Wistar PMRA # 2115485	Maternal toxicity: NOAEL: 10 mg/kg bw/day LOAEL: 75 mg/kg bw/day **75 mg/kg bw/day:** ↓ bwg, fc Developmental toxicity: NOAEL: 10 mg/kg bw/day LOAEL: 75 mg/kg bw/day **75 mg/kg bw/day:** ↑ post-implantation loss, early resorptions, late resorptions, ↓ live fetuses/dam, ↑ malformations (hyoid: misshapen arch, absent body, interrupted body, bent body; short intestine, 1 fetus; cleft palate, 1 fetus), ↑ visceral variations (misshapen nasopharynx lumen, displaced common carotid artery origin, tendonous region of diaphragm locally thinned), ↑ skeletal variations (additional ossification of squamosal or zygomatic process of the maxilla; zygomatic arch fusion; blue-stained focus(i) on the maxilla or mandible; accentuated curvature of the hyoid body; long cervical rib; rudimentary cervical rib; caudal displacement of the pelvic girdle; bilateral radius and ulna bent; cervical rib cartilage fused with thoracic rib 1 cartilage), ↑ skeletal variations (incompletely ossified sternebra 6; unilateral left supernumerary and rudimentary rib; unilateral right supernumerary and rudimentary rib; unilateral left and right supernumerary costal cartilage; ↓ non-ossification of the proximal phalanx of digit 2 on the left forelimb; ↑ interrupted costal cartilage 10; branched xiphoid cartilage, xiphoid cartilage with small hole; ↓ cervical vertebral body 2; ↑ non-ossification of the proximal phalanges on toes 2-4 of both feet) **No evidence of sensitivity of the young** **Serious effect in the young (mortality, malformations)**
Developmental toxicity, oral capsule Dutch rabbit, PMRA # 2115486, 2115487, 2405771, 2405772, 2405773	Maternal toxicity: NOAEL: 7.5 mg/kg bw/day LOAEL: 15 mg/kg bw/day **15 mg/kg bw/day:** mortality (1 doe, poor condition, not eating or drinking, weight loss, euthanized *in extremis*), bw loss (GD 6-19, uncorrected for gravid uterine wt; GD 0-29, corrected for gravid uterine wt), ↓ bwg (GD 0-29, uncorrected for gravid uterine wt), fc (22% GD 6-19)

Study Type/ Animal/ PMRA #	Study Results
	Developmental toxicity: NOAEL: 7.5 mg/kg bw/day LOAEL: 15 mg/kg bw/day **15 mg/kg bw/day:** ↑ early and late intrauterine deaths, complete litter resorptions, post-implantation loss, ↓ bw, number of litters, total and mean number of live fetuses, ↑ variations (13 bilateral lumbar, partially ossified frontals, interparietal partially to not ossified) **No evidence of sensitivity of the young** **Serious effect in the young (mortality)**
Genotoxicity Studies	
Bacterial Reverse Mutation Assay (Ames test) PMRA# 2115491	Cytotoxicity at 5000 µg/plate (±S9) in most strains **Negative**
Bacterial Reverse Mutation Assay (Ames test) PMRA# 2115492	In Expt. 1, cytotoxicity at 5000 µg/plate in TA1537 (-S9) and at ≥ 2500 µg/plate in TA 98 and TA1537 (+S9). In Expt. 2, cytotoxicity at ≥ 2500 µg/plate (±S9) in all strains except TA 1535, which exhibited cytotoxicity only at 5000 µg/plate (+S9) **Negative**
In vitro Mammalian Cell Assay (forward gene mutation) PMRA# 2115493	Cytotoxicity at ≥ 450 µg/mL (-S9) in Expt. 1, and at ≥ 600 µg/mL in Expt. 2 (± S9) **Negative**
In vitro Mammalian Clastogenicity Assay (chromosomal aberration) PMRA# 2115494	**Negative**
In vitro Cytogenetic Assay (chromosomal aberration) PMRA# 2115495	No cytotoxicity up to 250 µg/mL, the limit of solubility **Negative**
In vitro Mammalian Cell Assay (forward gene mutation) PMRA# 2115496	Cytotoxicity, and not assessed for gene mutations, in all experiments at ≥ 400 µg/mL (±S9), or at 600 µg/mL (Expt. 1, 4 hrs, +S9) **Negative**
In vivo micronucleus C57BL/6J/Alpk Mouse PMRA# 2115499	Cytotoxicity (↓ PCE:NCE ratio) at ≥ 93.8 mg/kg. **Negative**
In vivo cytogenetic Alpk Rat, PMRA# 2115500	At doses ≥ 70 mg/kg bw, ↓ bwg. **Negative**

Study Type/ Animal/ PMRA #	Study Results
Dominant lethal CD-1 Mouse, PMRA# 2115501	**Negative** **≥ 50 mg/kg bw/day**: ↓ bw (transient) (♂) **100 mg/kg bw/day**: Mortality by Day 5 of dosing (3/15 ♂), ↓ bw (♂)
In vivo unscheduled DNA synthesis Rat, Alpk PMRA# 2115502	**Negative**
Neurotoxicity Studies	
Acute neurotoxicity, oral gavage Sprague-Dawley Rats, PMRA# 2115508, 2115509	NOAEL = 250 mg/kg bw LOAEL = 750 mg/kg bw **≥ 750 mg/kg bw:** ↑ moribundity (4 ♂, 2 ♀), ↑ clinical signs (dehydration, chromorhinorrhea, urine-stained abdominal fur, ptosis, lost or impaired righting reflex, decreased motor activity, scant feces, hypothermia*, prostration*, flaccid/limp muscle tone*, laboured breathing or bradypnea*[†]; ungroomed coat, chromodacryorrhea, red or tan perioral substance hunched posture[†], slight ataxia[†] ♂; piloerection*, ♀), ↓ motor activity (number & total duration of movements), bw loss (Day 1-2), ↓ bwg (overall), ↓ fc (Day 1-3); ↓ bw, ↓ fc (Day 1-16) (♂) *Noted only in moribund animals [†] Noted at 8 h during FOB **No evidence of selective neurotoxicity**
90-Day dietary neurotoxicity Rat PMRA# 2115510, 2115512	NOAEL = 84.3/97.6 mg/kg bw/day ♂/♀ LOAEL =172.1/185.0 mg/kg bw/day ♂/♀ **172.1/185.0 mg/kg bw/day:** ↓ fc, ↓ bw, ↓ bwg; ↓ hindlimb grip strength (Wk 2) (♂); ↓ brain wt (absolute) (♀) **No evidence of selective neurotoxicity**
Special Studies	
28-Day dietary immunotoxicity (AFC assay) Mouse PMRA# 2379412	NOAEL = 50 ppm (9.8 mg/kg bw/day) LOAEL = 250 ppm (46.8 mg/kg bw/day) **≥ 46.8 mg/kg bw/day:** ↓ MCV (*non-adverse*), ↑ liver wt (44%) **No evidence of immunotoxicity**

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Flutriafol

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary, general population	1-year and 90-day toxicity studies in the dog (co-critical)	NOAEL = 5.0 mg/kg bw/day Body weight loss	100
	ARfD = 0.05 mg/kg bw		
Acute dietary, females 13-49 years of age	Developmental toxicity study in the rabbit	NOAEL = 7.5 mg/kg bw/day Reduced body weight, number of live fetuses, increased complete litter resorptions, post-implantation loss, and skeletal variations	300
	ARfD = 0.025 mg/kg bw		
Repeated dietary, general population	1-year and 90-day toxicity studies in the dog (co-critical)	NOAEL = 5.0 mg/kg bw/day Body weight loss	100
	ADI = 0.05 mg/kg bw/day		
Repeated dietary, females 13-49 years of age	Developmental toxicity study in the rabbit	NOAEL = 7.5 mg/kg bw/day Reduced body weight, number of live fetuses, increased complete litter resorptions, post-implantation loss, and skeletal variations	300
	ADI = 0.025 mg/kg bw/day		
Short- to Intermediate-term dermal[2] and inhalation[3]	Developmental toxicity study in the rabbit	NOAEL = 7.5 mg/kg bw/day Reduced body weight, number of live fetuses, increased complete litter resorptions, post-implantation loss, and skeletal variations	300
Cancer	No evidence of oncogenicity.		

[1] CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary assessments; MOE refers to a target MOE for occupational assessments. [2] An oral NOAEL was selected and a dermal absorption factor of 20% was used in route-to-route extrapolation. [3] An oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 5 Integrated Food Residue Chemistry Summary

Nature of the Residue – Apples, Rapeseed, Sugar Beets				**PMRA # 2115642, 2115643, 2115645, 2115648, 2115650**		
Apples	1 foliar application of 125 g/L SC formulation made at early fruit development at 118 g a.i./ha; PHI of 64 days.					
Radiolabel Position	**[Triazole-3,5-^{14}C]**			**[Carbinol-^{14}C]**		
Crop	**Apple**			**Apple**		
Fraction	**Fruit**	**Foliage**		**Fruit**	**Foliage**	
Overall TRR (mg/kg)	0.065	4.182		0.041	na	
Major Metabolites (>10% of TRR)	flutriafol	flutriafol		flutriafol	na	
Minor Metabolites (<10% of TRR)	none	none		none	na	
Sugar beets	1 foliar application of 125 g/L SC formulation made at 129-133 g ai/ha.					
Radiolabel Position	**[Triazole-3,5-^{14}C]**			**[Carbinol-^{14}C]**		
Crop	**Sugar beet**			**Sugar beet**		
Fraction	**Roots**	**Roots**	**Roots**	**Roots**	**Roots**	**Roots**
Timing (DAT)	0	16	21	0	16	21
Overall TRR (mg/kg)	0.001	0.003	0.009	<0.001	0.005	0.005
Sugar beet roots were not further analyzed for identification and/or characterization.						
Fraction	**Tops**	**Tops**	**Tops**	**Tops**	**Tops**	**Tops**

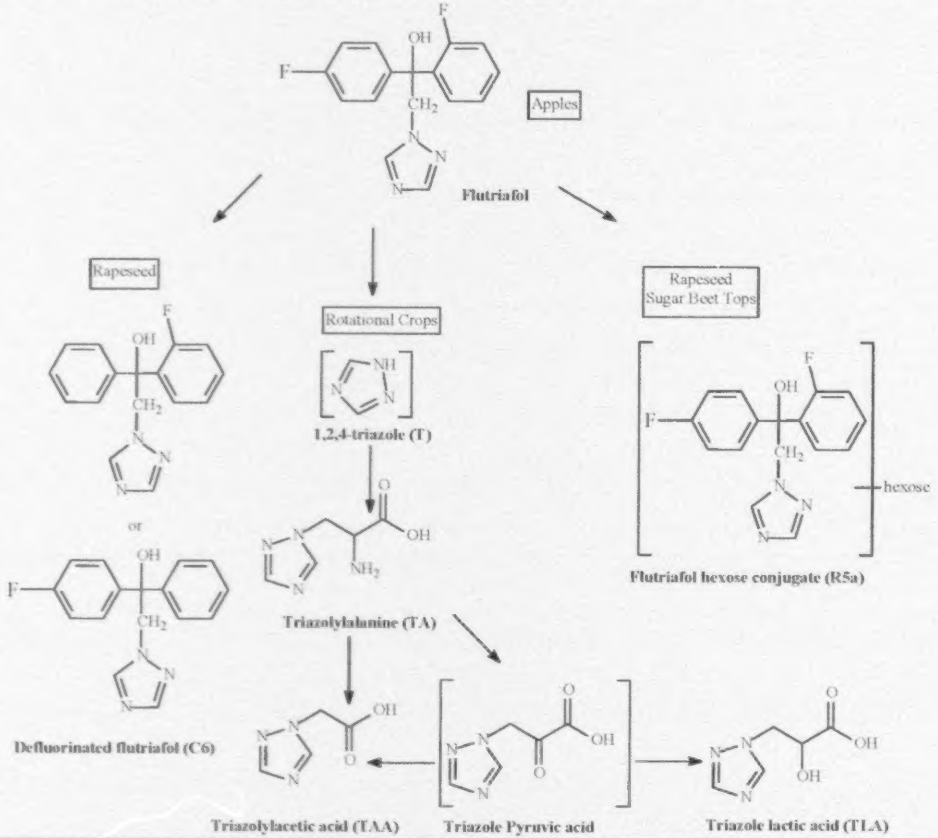
Nature of the Residue – Apples, Rapeseed, Sugar Beets				**PMRA # 2115642, 2115643, 2115645, 2115648, 2115650**		
Timing (DAT)	0	16	21	0	16	21
Overall TRR (mg/kg)	1.368	0.342	0.747	1.273	0.381	0.596
Major Metabolites (>10% of TRR)	flutriafol			flutriafol		
Minor Metabolites (<10% of TRR)	none	R5a	R5a	none	R5a	R5a

Rapessed	1 foliar application of 125 g/L SC formulation made at early pod set at 115-118 g ai/ha.									
Radiolabel Position	**[Triazole-3,5-^{14}C]**					**[Carbinol-^{14}C]**				
Crop	**Rapeseed**					**Rapeseed**				
Fraction	**Forage**	**Foliage**		**Pod**	**Seed**	**Forage**	**Foliage**		**Pod**	**Seed**
Timing (DAT)	0	14	42	14	42	0	14	42	14	42
Overall TRR (mg/kg)	0.782	1.165	0.246	0.751	1.316	1.497	1.601	0.355	0.779	0.729
Major Metabolites (>10% of TRR)	flutriafol	flutriafol	flutriafol	flutriafol C6	flutriafol	Flutriafol	flutriafol	flutriafol	flutriafol C6	flutriafol
Minor Metabolites (<10% of TRR)	none	C6	C6	R5a	C6, R5a	None	C6	C6	R5a	C6, R5a

Confined Accumulation in Rotational Crops – Lettuce, Radish and Wheat					**PMRA # 2115750, 2115756**		
Crop matrices were rotated following treatment of bare soil at 246 g ai/ha in outdoor field plots.							
Radiolabels		**[Triazole-3,5-^{14}C]-Flutriafol**			**[Carbinol-^{14}C]-Flutriafol**		
PBI (days)		**30**	**120**	**365**	**30**	**120**	**365**
Lettuce	**Overall TRR (mg/kg)**	0.076	0.075	0.123	0.048	0.050	0.019
Major Metabolites (>10% of TRR)		flutriafol, TA, TLA	flutriafol, TA, TLA	flutriafol, TA, TLA	flutriafol	na	flutriafol
Minor Metabolites (<10% of TRR)		none	none	TAA	none	none	none
Radish Roots	**Overall TRR (mg/kg)**	0.066	0.051	0.059	0.023	0.020	0.008
Major Metabolites (>10% of TRR)		flutriafol, TA	flutriafol, TA	flutriafol, TA	na	na	na
Minor Metabolites (<10% of TRR)		TLA	TLA	TLA	na	na	na
Radish Tops	**Overall TRR (mg/kg)**	0.177	0.084	0.107	0.060	0.048	0.071
Major Metabolites (>10% of TRR)		flutriafol, TA	flutriafol, TA	flutriafol, TA	flutriafol	na	flutriafol
Minor Metabolites (<10% of TRR)		TLA	TLA	TLA	none	na	none
Wheat Grain	**Overall TRR (mg/kg)**	0.648	0.528	0.440	0.032	0.028	0.011
Major Metabolites (>10% of TRR)		TA, TAA	TA, TAA	TA, TAA	na	na	flutriafol
Minor Metabolites (<10% of TRR)		flutriafol	flutriafol	flutriafol	na	na	none
Wheat Forage	**Overall TRR (mg/kg)**	0.230	0.242	0.075	0.130	0.130	0.061
Major Metabolites (>10% of TRR)		flutriafol, TA	flutriafol, TA	flutriafol, TLA, TA	na	na	flutriafol
Minor Metabolites (<10% of TRR)		TLA	TLA	TAA	na	na	none
Wheat Hay	**Overall TRR (mg/kg)**	0.668	0.497	0.191	0.357	0.290	0.083
Major Metabolites (>10% of TRR)		flutriafol, TA	flutriafol, TA	flutriafol, TLA, TA, TAA	flutriafol	flutriafol	flutriafol
Minor Metabolites (<10% of TRR)		TLA, TAA	TLA, TAA	None	none	none	none
Wheat Straw	**Overall TRR (mg/kg)**	1.749	1.395	0.798	1.129	1.220	0.480

Major Metabolites (>10% of TRR)	flutriafol, TLA, conjugated TA	flutriafol, TLA, conjugated TA	flutriafol, TLA	flutriafol	flutriafol	flutriafol
Minor Metabolites (<10% of TRR)	TAA, TA	TAA, TA	TAA, TA	none	none	none

Proposed Metabolic Profile in Plants (Primary and Secondary Crops)


Apples
Flutriafol
Rapeseed
Rotational Crops
Rapeseed
Sugar Beet Tops
1,2,4-triazole (T)
or
Defluorinated flutriafol (C6)
Triazolylalanine (TA)
Flutriafol hexose conjugate (R5a)
hexose
Triazolylacetic acid (TAA)
Triazole Pyruvic acid
Triazole lactic acid (TLA)

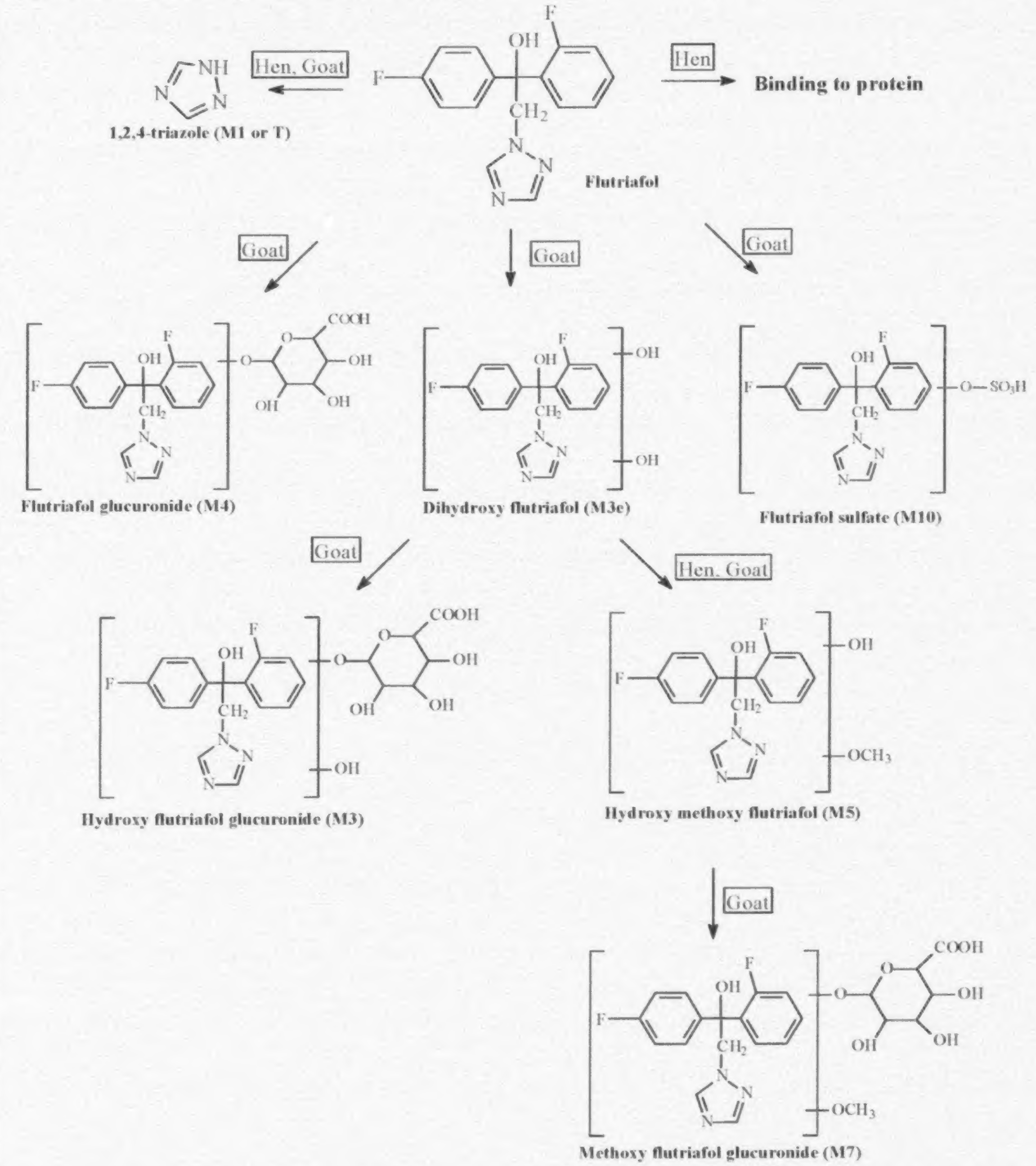
Nature of the Residue in Laying Hens	**PMRA # 2115641**

Laying hens were dosed once daily orally for 7 consecutive days with [triazole-3,5-^{14}C]-flutriafol and [carbinol-^{14}C]-flutriafol at 13.9 ppm and 11.6 ppm in the diet, respectively. Eggs were collected twice daily throughout the study, and muscle (composite of breast and thigh), abdominal fat, and liver were collected at sacrifice, 20-24 hours after the final dose was administered.

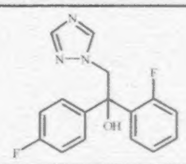
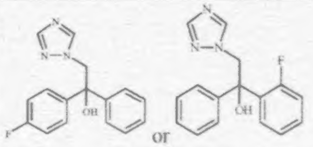
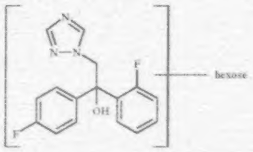
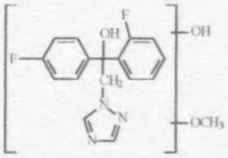
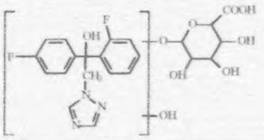
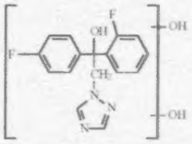
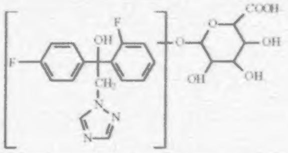
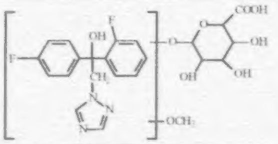
Matrices	**[Triazole-3,5-^{14}C]-Flutriafol**		**[Carbinol-^{14}C]-Flutriafol**	
	TRR (mg/kg)	**% of AD**	**TRR (mg/kg)**	**% of AD**
Excreta (total)	--	89.7	--	91.2
Other, GI and contents	--	1.9	--	1.4
Muscle (composite)	0.064	--	0.011	--
Fat	0.035	--	0.016	--
Liver	0.411	--	0.359	--
Eggs (Day 8)	0.204	--	0.134	--
Sum of AD (%)	**91.6**		**92.6**	
Metabolites identified	**Major Metabolites (>10% of the TRR)**		**Minor Metabolites (<10% of the TRR)**	
Radiolabel Position	**[Triazole-3,5-^{14}C]**	**[Carbinol-^{14}C]**	**[Triazole-3,5-^{14}C]**	**[Carbinol-^{14}C]**
Eggs	flutriafol, T	flutriafol	M5	M5
Muscle (composite)	T	--	M5	M5
Fat	flutriafol, T	flutriafol	M5	--
Liver	T	--	flutriafol, M5	flutriafol, M5

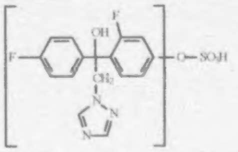
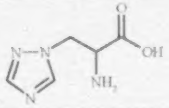
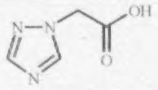
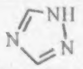
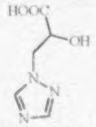
Nature of the Residue in Lactating Goats – 30-31 mg/kg			**PMRA # 2276281**	
Two lactating goats were each dosed once daily for 5 consecutive days by gelatin capsule with [triazole-3,5-^{14}C]-flutriafol and [carbinol-^{14}C]-flutriafol at 30-31 mg/kg (dry-weight basis). Samples of excreta were collected daily and milk was collected twice daily. Bile, blood, gastrointestinal tract with contents, muscle (composite), fat (composite), liver, and kidney were collected at sacrifice, 20-22 hours after the final dose was administered.				
Matrices	**[Triazole-3,5-^{14}C]-Flutriafol**		**[Carbinol-^{14}C]-Flutriafol**	
	TRRs (mg/kg)	**% of AD**	**TRRs (mg/kg)**	**% of AD**
Urine	--	30.03	--	34.67
Feces	--	55.32	--	53.77
GI tract	--	2.15	--	6.84
Cage wash	--	0.04	--	--
Bile	4.68	0.03	13.54	0.05
Blood	0.047	<0.01	0.044	<0.01
Muscle (composite)	0.020	<0.01	0.023	<0.01
Fat (composite)	0.011	<0.01	0.017	<0.01
Kidney	0.123	0.01	0.304	0.02
Liver	0.607	0.22	0.631	0.22
Milk (Day 6)	0.029	0.05	0.038	0.05
Skim milk (Day 6)	0.029	--	0.037	--
Cream (Day 6)	0.027	--	0.050	--
Sum of AD (%)	**87.88**		**95.65**	
Metabolites identified	**Major Metabolites (>10% of the TRR)**		**Minor Metabolites (<10% of the TRR)**	
Radiolabel Position	**[Triazole-3,5-^{14}C]**	**[Carbinol-^{14}C]**	**[Triazole-3,5-^{14}C]**	**[Carbinol-^{14}C]**
Skim milk	T, M3, M3e	M3, M3e	flutriafol, M5, M7	flutriafol, M5, M7, M10
Cream	T, M3	M3, M10	flutriafol, M5	flutriafol, M5
Liver	--	--	flutriafol, T, M3, M3e, M4, M5, M7	flutriafol, M3, M3e, M4, M5, M7
Kidney	M3, M4	M3, M4, M7	T, M3e, M5, M7	flutriafol, M3e, M5
Muscle (composite)	T, M3	M4 (flank)	--	M3, M4 (loin), M7 (loin)
Fat (composite)	T	flutriafol	flutriafol, M3	--

Proposed Metabolic Pathway in Livestock (Goat and Hen)


Hen, Goat
1,2,4-triazole (M1 or T)
Hen
Binding to protein
Flutriafol
Goat
Goat
Goat
Flutriafol glucuronide (M4)
Dihydroxy flutriafol (M3c)
Flutriafol sulfate (M10)
Goat
Hen, Goat
Hydroxy flutriafol glucuronide (M3)
Hydroxy methoxy flutriafol (M5)
Goat
Methoxy flutriafol glucuronide (M7)

List of Metabolites Identified in Metabolism Studies

Common name (code)	Chemical name	Chemical structure	Found in metabolism studies
Flutriafol	(*RS*)-2,4'-difluoro-α-(1*H*-1,2,4-triazol-1-ylmethyl)benzhydril alcohol		Plants, goat, hen
Defluorinated flutriafol (C6)	Not provided	 N N–N OH F or N N–N F OH	Plants
Flutriafol hexose conjugate (R5a)	Not provided	 N N–N F hexose OH F	Plants
Monohydroxy flutriafol derivatives (M5)	Not provided	 F OH –OH F CH₂ N N N –OCH₃	Hen, goat
Hydroxy flutriafol glucuronide (M3)	Not provided	 COOH F OH O –O –OH F CH₂ OH OH N N N –OH	Goat
Dihydroxy flutriafol (M3e)	Not provided	 F OH –OH F CH₂ N N N –OH	Goat
Flutriafol glucuronide (M4)	Not provided	 COOH F O OH –O –OH F CH₂ OH OH N N N	Goat
Methoxy flutriafol glucuronide (M7)	Not provided	 COOH F O OH –O –OH F CH₂ OH OH N N N –OCH₃	Goat

Common name (code)	Chemical name	Chemical structure	Found in metabolism studies
Futriafol sulfate (M10)	Not provided		Goat
Triazolylalanine (TA)	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid		Plants
Triazolylacetic acid (TAA)	1*H*-1,2,4-triazol-1-ylacetic acid		Plants
1,2,4-Triazole (T or M1)	1*H*-1,2,4-triazole		Goat, Hen, Rotational crops (as intermediate)
Triazole lactic acid (TLA)	1,2,4-triazole-1-lactic acid		Rotational crops

Freezer Storage Stability in Plant Matrices **PMRA # 2115916-2115923, 2115700**

Samples were stored at -18°C. The data can be extended to crop field trials and processing studies to cover the maximum storage intervals observed.

Commodity Categories	Representative Commodities	Demonstrated Duration of Stability (Months)
High-water content	Cabbage, apples, wheat forage	12
	Apple juice	2.1
	Apple pomace	4.3
High-oil content	Rapeseed	12
	Soybean (seeds)	5
	Soybean (refined oil)	2
High-protein content	Peas	12
	Soybean (meal and hulls)	1.7
High-starch content	Wheat (straw, grain), sugar beet roots	12

Freezer Storage Stability in Animal Matrices **PMRA # 2115779 (poultry); 2398787 (bovine)**

Samples were stored in freezer at -20°C. The demonstrated duration of stability covers the maximum storage interval observed in the livestock feeding studies.

Species	Commodity	Demonstrated Duration of Stability (Days)
Poultry	Eggs	117
	Muscle	120
	Fat	116
	Liver	369
Bovine	Milk	146
	Muscle	372
	Liver	369
	Kidney	365
	Fat	370

Crop Field Trials – Domestic Crops	**PMRA # 2115698, 2115699, 2115700-2115703**			
Crops:	**Apples**	**Dry soybeans**	**Grapes**	**Strawberries**
Number of Trials:	20	21	17	10
Trial Locations:	Conducted in representative NAFTA growing regions.			
Formulation Type:	125 g/L SC			
Application Type:	Foliar applications using ground equipment.			
Adjuvant Use:	none	NIS	none	none
Residue Decline Trend:	↓ Residues ↑PHI	↓ Residues ↑PHI (trial 1) ↕ Residues ↑PHI (trial 2)	↓ Residues ↑PHI	↓ Residues ↑PHI
Registered Maximum Rate (g ai/ha/season):	256	256	256	256
Study X-fold Approved GAP	2.8	1.0	3.6	2.0

Commodity	**Max. Appl. Rate [g ai/ha]**	**PHI (days)**	**Flutriafol Residue Levels (ppm)**							
			n	**Min.**	**Max.**	**LAFT**	**HAFT**	**Median**	**Mean**	**SD**
Apples	720	13-15	40	0.013	0.138	0.018	0.128	0.066	0.071	0.035
Dry soybeans	260	20-23; 27	42	<0.010	0.306	0.010	0.303	0.051	0.072	0.071
Grapes	920	14	34	0.053	0.885	0.066	0.861	0.291	0.334	0.186
Strawberries	510	0	20	0.094	0.781	0.140	0.704	0.428	0.444	0.191

Crop Field Trials - Imported Crops	**PMRA # 2115704, 2115706, 2115708, 2115709, 2115711, 2115712, 2115713, 2115716, 2115717**					
Crops:	**Bananas**	**Field corn**	**Pears**	**Peanuts**	**Sugar beets**	**Stone fruits**
Number of Trials:	12	20	6	13	12	12 (peaches); each 8 (tart/ sweet cherries, plums)
Trial Locations:	Appropriate NAFTA growing regions. Representative regions of Central/South America for bananas.					
Formulation Type:	125 g/L SC					
Application Type:	Foliar applications using ground equipment in spray volumes (dilute or concentrated). For bananas, applications were made using ground equipment in a manner designed to simulate aerial sprays.					
Adjuvant Use:	Spray oil/emulsifier	NIS	none	NIS	none	none
Residue Decline Trend:	↓ Residues ↑PHI					
Registered Maximum Rate (g ai/ha/season):	800	255	476	492	256	463
Study X-fold of Registered GAP	1.3	1.0	1.5	1.3	1.5	1.1

Crop	Max Appl. Rate [g ai/ha]	PHI (days)	Flutriafol Residue Levels (ppm)							
			n	Min.	Max.	LAFT	HAFT	Median	Mean	SD
Bananas (unbagged)	1010	0	24	<0.010	0.199	0.015	0.175	0.091	0.089	0.056
Field corn forage	260	0	40	0.323	3.47	0.332	2.74	1.49	1.52	0.70
Field corn grain		6-9	40	<0.010	<0.01	0.010	0.010	0.010	0.010	0.000
Field corn stover		6-9	40	0.010	9.51	0.020	8.90	3.69	4.30	2.31
Pears	730	14	12	0.029	0.262	0.034	0.230	0.133	0.145	0.080
Peanut nutmeat	640	6-8	26	<0.010	0.089	0.010	0.081	0.022	0.027	0.019
Peanut hay		6-8	26	0.63	10.2	0.740	8.92	2.83	4.10	2.99
Sugar beet tops	390	13-15	24	0.02	1.830	0.028	1.775	0.624	0.672	0.534
Sugar beet roots		13-15	24	<0.010	0.062	0.010	0.053	0.013	0.019	0.016
Stone fruits										
Peaches	510	6-7	24	0.052	0.417	0.052	0.407	0.168	0.183	0.086
Tart cherries	510	7	16	0.230	0.492	0.238	0.469	0.341	0.353	0.079
Sweet cherries	510	7	16	0.145	0.660	0.169	0.590	0.318	0.352	0.140
Plums	510	7	16	0.019	0.252	0.022	0.224	0.079	0.086	0.064

Residue Data in Rotational Crops- Field Corn, Sweet Corn, Cotton | **PMRA # 2115769, 2115772, 2115774, 2115776**

Field corn, sweet corn, and cotton were planted in a soybean field previously treated with flutriafol in NAFTA growing regions using ground sprayer equipment (140-300 L/ha) with retreatment intervals (RTIs) of 12-21 days. Data for cotton is not reported as it is not relevant to the Canadian scenario.

Crop	Total App. Rate (g ai/ha)	PBI (days)	Flutriafol Residue Levels (ppm)							
			n	Min.	Max.	LAFT	HAFT	Median	Mean	SD
Field Corn Forage	243-263	153-287	40	<0.010	0.091	<0.010	0.083	0.010	0.017	0.018
Field Corn Stover			40	<0.010	0.063	<0.010	0.056	0.010	0.016	0.013
Field Corn Grain			40	<0.010	<0.010	<0.010	<0.010	<0.010	<0.010	NA
Sweet Corn Forage	190-262	207-288	24	<0.010	0.034	<0.010	0.030	0.010	0.012	0.006
Sweet Corn Stover			24	<0.010	0.040	<0.010	0.035	0.011	0.015	0.008
Sweet Corn Ears			24	<0.010	<0.010	<0.010	<0.010	<0.010	<0.01	NA

Based on the results of the field accumulation study, a plant-back interval of 150 days is recommended for field corn (extended to popcorn), and 200 days for sweet corn. Labeled crops may be rotated at any time. Unlabeled crops may be rotated after one year.

Processed Food and Feed –
Apples, Plums, Dry Soybeans, Grapes, Peanuts, Field Corn | **PMRA # 2115699, 2115708, 2115717, 2115700, 2115702, 2115713**

Processing studies were conducted using samples from crop field trials conducted in NAFTA growing regions. The broadcast foliar applications were made with 125 g/L SC.

RAC	Processed Commodity	Total Rate (kg a.i./ha)	X-Fold GAP	PHI (days)	Average Residues (ppm)	Processing Factor	RAC HAFT (ppm)	AR (ppm)
Apples	Fruit (RAC)	1.09	4.3	14	0.113	--	0.128	--
	Juice				0.048	0.4		0.05
	Wet pomace				0.209	1.9		0.24
Plums	Fruit (RAC)	2.55	5.0	7	0.644	--	0.224	--
	Prunes				1.400	2.2		0.49
Peanuts	Nutmeat (RAC)	3.19	6.5	7	0.194	--	0.081	--
	Meal				0.148	0.8		0.06
	Refined oil				0.260	1.3		0.11
Dry Soybeans	Seed (RAC)	0.255	1.0	21	0.068	--	0.303	--
	AGF				0.301	4.4		1.3

RAC	Processed Commodity	Total Rate (kg a.i./ha)	X-Fold GAP	PHI (days)	Average Residues (ppm)	Processing Factor	RAC HAFT (ppm)	AR (ppm)
	Seed (RAC)	1.28	5.0	21	0.284	--		--
	Meal				0.392	1.4		0.4
	Hulls				0.275	0.97		0.3
	Refined oil				0.369	1.3		0.4
Grapes	Fruit (RAC)	1.80	7.0	14	0.397	--	0.861	--
	Sun-dried raisins				1.110	2.8		2.4
	Raisins				1.090	2.7		2.3
	Juice				0.251	0.6		0.5
Field corn	Grain (RAC)	0.254	1.1	7	<0.01	--	0.01	--
	AGF				0.041	4.1		0.04
	Grain (RAC)	1.28	5.7	7	<0.01	--		--
	Grits				<0.01	1		0.01
	Meal				<0.01	1		0.01
	Flour				<0.01	1		0.01
	Starch				<0.01	1		0.01
	Refined oil (wet)				0.015	1.5		0.015

Livestock Feeding Study – Dairy Cattle **PMRA # 2276283-2276285**

Lactating dairy cows were administered flutriafol orally once daily for 29 consecutive days at dose levels of 5 ppm, 16 ppm, and 50 ppm on a dry-weight basis, corresponding to 29-fold, 94-fold, and 294-fold of the estimated dietary burden for dairy cattle, respectively. Only the values from the feeding level closest to the estimated dietary burden are reported. Whole milk samples were not analyzed at the 5.0 ppm feeding level. However, residues of flutriafol were <0.01 ppm in whole at the 16- and 50 ppm feeding levels.

Commodity	Feeding Level (ppm)	HR (ppm)	DB based on Dairy Cattle (ppm)	AR (ppm)
Whole milk	5 16 (whole milk only)	<0.01	0.17	0.0001
Fat		<0.01		0.0003
Liver		0.444		0.015
Kidney		<0.01		0.0003
Muscle		<0.01		0.0003

Livestock Feeding – Laying Hens **PMRA # 2115779**

Laying hens were administered flutriafol orally once daily for 29 consecutive days at dose levels of 0.45 ppm, 1.34 ppm, and 4.48 ppm on a dry-weight basis, corresponding to 22.5-fold, 67-fold, and 224-fold of the estimated dietary burden for poultry, respectively. Only the values from the feeding level closest to the estimated dietary burden are reported.

Commodity	Feeding Level (ppm)	HR (ppm)	DB (ppm)	AR (ppm)
Whole Egg	0.45	<0.01	0.02	0.0004
Fat		<0.01		0.0004
Liver		<0.01		0.0004
Muscle		<0.01		0.0004

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

Plant Studies	
Residue Definition for Enforcement and Risk Assessment Primary crops (apple, sugar beet, rapeseed) Rotational crops (radish, wheat, lettuce)	Flutriafol
Metabolic Profile in Diverse Crops	Similar
Animal Studies	
Animals	Ruminant and Poultry
Residue Definition for Enforcement and Risk Assessment (goat and hen)	Flutriafol
Metabolic Profile in Animals (goat, hen, rat)	More extensive in goat and rat.
Fat Soluble Residue	Yes

Basic and refined chronic non-cancer dietary exposure analysis **ADI = 0.05 mg/kg bw/day** **$\text{ADI}_{\text{females 13-49 yrs}}$ 0.025 mg/kg bw** **Estimated chronic drinking water concentration (EEC):** **Level 1: 0.196 ppm**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**		
		Food Alone		**Food and Water**
		Basic	**Refined**	**Level 1 EEC**
				Refined
	All infants < 1 year	16.3	1.9	29.0
	Children 1–2 years	25.5	3.1	15.3
	Children 3 to 5 years	16.0	2.1	13.6
	Children 6–12 years	6.8	1.0	8.9
	Males 13–19 years	2.7	0.4	6.4
	Males 20–49 years	2.1	0.4	8.1
	Adults 50+ years	2.6	0.5	8.6
	Females 13-49 years	4.6	0.8	16.1
Basic and refined acute dietary exposure analysis, 95th percentile **ARfD = 0.05 mg/kg bw/day** **$\text{ARfD}_{\text{females 13-49 yrs}}$= 0.025 mg/kg bw** **Estimated acute drinking water concentration (EEC):** **Level 1: 0.198 ppm**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**		
		Food Alone		**Food and Water**
		Basic	**Refined**	**Level 1 EEC**
				Refined
	All infants < 1 year	62.7	16.6	82.3
	Children 1–2 years	85.7	27.1	49.0
	Children 3 to 5 years	55.2	18.7	39.8
	Children 6–12 years	25.7	9.2	25.5
	Males 13–19 years	11.1	3.8	18.7
	Males 20–49 years	8.7	3.4	20.8
	Adults 50+ years	9.5	3.7	19.1
	Females 13-49 years	19.4	7.4	42.1

Table 7 Summary of physico-chemical properties of flutriafol relevant to the environment

Property	Value	Comments
Water solubility	95 mg/L (20 °C)	Soluble in water
Vapour pressure	9×10^{-4} Pa (60 °C) 2×10^{-4} Pa (50 °C) 3×10^{-5} Pa (40 °C) 3×10^{-6} Pa (30 °C) 4×10^{-7} Pa (20 °C) 4×10^{-8} Pa (10 °C)	Low volatility
Henry's Law Constant	1.27×10^{-6} Pa × m^3/mole (20 °C); 1.3×10^{-11} atm × m^3/mole (20 °C); $1/H = 1.9 \times 10^{9}$ (reviewer-calculated)	Low potential to volatilize from moist soils or from water.
log K_{OW}	2.3 (20 °C)	Not expected to bioaccumulate
pK_a	$pK_a = 2.3 \pm 0.2$ (25 °C)	Anion under environmentally-relevant conditions
UV-visible absorption	Maximum molecular absorption at approximately 205 nm. No absorption between 280 nm and 400 nm.	Low potential for direct phototransformation

Table 8 Fate and behaviour in the terrestrial environment

Property	Test substance	Value	Comments	PMRA#
Abiotic transformation				
Hydrolysis (25°C)	[^{14}C]-triazole labelled flutriafol (>97.3%)	Half-life: Stable at pH 5, 7 and 9	Not an important route of dissipation	2115624
Phototransformation on soil	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (≥98%)	Half-life: could not be calculated due to limited transformation.	Not an important route of dissipation	2115625
Phototransformation on soil (25°C)	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (≥98.7%)	Half-life: 72.2 d (continuous irradiation, combined labels), equivalent to 177 solar days at 40°N	Not an important route of dissipation	2115627
Phototransformation in air	n/a	DT_{50} in air of 1.1 days, derived by the Atkinson method of calculation assuming an OH radical	Study not submitted but results are presented in	2149708

Property	Test substance	Value	Comments	PMRA#
		concentration in the troposphere of 1.5 × 10^6 molecules/cm^3	PMRA 2149708.	
Biotransformation				
Biotransformation in aerobic soil (25°C)	[^{14}C]-triazole labelled flutriafol (≥98.8%)	Sandy loam (North Dakota): DT$_{50}$: 4807 d; DT$_{90}$: 15970 d (SFO)	Persistent	2115583
Biotransformation in aerobic soil (20°C)	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (99%)	Sandy clay loam (18 Acres): DT$_{50}$: 1090 d; DT$_{90}$: 3621 d (SFO, combined labels)	Persistent	2115584, 2115618, 2115586
		Loamy sand (Frensham): DT$_{50}$: 1162 d; DT$_{90}$: 3861 d (SFO, combined labels)	Persistent	
	[^{14}C]-triazole labelled flutriafol (99%)	Clay loam (Boxford): DT$_{50}$: 811 d; DT$_{90}$: 2694 d (SFO)	Persistent	2115584, 2115618, 2115586
		Sandy clay loam (Chalgrove): DT$_{50}$: 3492 d; DT$_{90}$: 11599 d (SFO)	Persistent	
		Loamy sand (Horsley): DT$_{50}$: 672 d; DT$_{90}$: 2231 d (SFO)	Persistent	
		Sandy loam (Flexford): DT$_{50}$: 2464 d; DT$_{90}$: 8185 d (SFO)	Persistent	
	flutriafol (purity not reported)	Sand (Speyer 2.2): DT$_{50}$ and DT$_{90}$ not calculated due to limited transformation	Persistent	2115585, 2115586
		Sand (Speyer 2.3): DT$_{50}$: 3176 d (slow half-life: 3500 d); DT$_{90}$: 11309 d (DFOP)	Persistent	
		Loamy sand (Warfield): DT$_{50}$: 1702 d; DT$_{90}$: 5654 d (SFO)	Persistent	
Biotransformation in anaerobic soil (20°C)	[^{14}C]-triazole labelled flutriafol (99%)	Sandy clay loam (18 Acres): DT$_{50}$: 1071 d; DT$_{90}$: 3559 d (SFO)	Persistent	2115584, 2115618
Mobility				
Adsorption /	[^{14}C]-triazole	Roquefort loamy sand	Moderate	2115591

Property	Test substance	Value	Comments	PMRA#
desorption in soil	labelled flutriafol ($\geq$97%)	K_d: 10.11 mL/g; K_{OC}: 409.4 mL/g; K_f: 9.754; K_{fOC}: 395; 1/n: 0.97	mobility	
		Mussig clay loam K_d: 5.801 mL/g; K_{OC}: 124.2 mL/g; K_f: 5.766; K_{fOC}: 123; 1/n: 0.94	High mobility	
	[^{14}C]-triazole labelled flutriafol (>99%)	Hyde Farm loam Adsorption: K_d: 5.827 mL/g; K_{OC}: 306.7 mL/g; K_f: 5.7; K_{fOC}: 304; 1/n: 0.92 Desorption: K_{des}: 4.282; $K_{f\text{-}des}$: 4.775 ; 1/n-des: 0.63	Moderate mobility	2115594
		Lillifield coarse sand Adsorption: K_d: 1.394 mL/g; K_{OC}: 309.9 mL/g; K_f: 1.3; K_{fOC}: 295; 1/n: 0.88 Desorption: K_{des}: 0.583; $K_{f\text{-}des}$: 1.229; 1/n-des: 0.272	Moderate mobility	
		Bayonvillers silt loam Adsorption: K_d: 1.864 mL/g; K_{OC}: 155.3 mL/g; K_f: 1.9; K_{fOC}: 157; 1/n: 0.92 Desorption: K_{des}: 1.48; $K_{f\text{-}des}$: 1.667; 1/n-des: 0.693	Moderate mobility	
	[^{14}C]-triazole labelled flutriafol (99.8%)	North Dakota sandy loam K_d: 2.738 mL/g; K_{OC}: 195.6 mL/g; K_f: 3.22; K_{fOC}: 230; 1/n: 0.795	Moderate mobility	2115589
		North Dakota clay loam K_d: 9.948 mL/g; K_{OC}: 248.7 mL/g; K_f: 11.11 ; K_{fOC}: 278; 1/n:	Moderate mobility	

Property		Test substance	Value	Comments	PMRA#
			0.781		
Effect of time on sorption in soil		Flutriafol (99%)	Some evidence of stronger sorption of flutriafol with time.	Supplemental information	2115596
		[^{14}C]-triazole labelled flutriafol (96.05%)	Time dependent sorption experiment: Sorption increased with time of ageing Concentration dependent sorption experiment: Sorption increased with decreasing test concentration	Supplemental information	2115597
Soil leaching		[^{14}C]-triazole labelled flutriafol (99%)	Not detected in the leachate after eluting with the equivalent of 320 mm of 'rainfall' (80 mL 0.01M CaCl$_2$) over a period of 10 to 27 days.	Supplemental information	2115599
Volatilization		[^{14}C]-triazole labelled flutriafol formulated as a suspension concentrate	<3% volatilized from soil and plant surfaces after 24 hours	Study not submitted but results cited in PMRA 2210920	2210920
Field studies					
New York site (relevant to Canada)	Field dissipation	Flutiafol SC (EP 125 g a.i./L)	No significant dissipation from bareplots; cropped plots DT$_{50}$: 635 days; at the end of 24 months, 69% in bareplots and 64% in cropped plots remained Other US studies DT$_{50}$: 195-437 days for bareplots and 318-495 days for cropped plots	Persistent	2115600
	Accumulation		DT$_{90}$: > 2000 days (cropped plots) Other US studies: 646-153 days bare plots and 1055-1645 days for cropped plots	Potential for residue carryover	
	Field leaching		Residues detected beyond 30 cm soil depth	Potential foe leaching	

Property		Test substance	Value	Comments	PMRA#
	Transformation products		Not tracked as no major transformation products were detected in laboratory studies		

Table 9 Fate and behaviour in the aquatic environment

Study type	Test material	Value		Comments	PMRA#
Abiotic transformation					
Hydrolysis (25°C)	[^{14}C]-triazole labelled flutriafol (>97.3%)	Half-life: Stable at pH 5, 7 and 9		Not expected to be an important route of dissipation	2115624
Phototransformation in water (25°C)	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (≥96.1%)	Half-life: Stable in aqueous buffer at pH 7 when exposed to artificial light for 9 days (equivalent to 66 days of Florida sunshine)		Direct phototransformation is not expected to be an important route of dissipation (half-life >7 d)	2115630
	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (≥98.2%)	Half-life: Stable in sterile pond water when exposed to artificial light for 15 days (equivalent to 33 days of natural midsummer sunlight at 30-40°N).		Direct phototransformation is not expected to be an important route of dissipation (half-life >7 d)	2115635
Quantum yield	Flutriafol (98.8%)	Quantum yield was zero (no measurable phototransformation)		Supplemental information	2115631
Biotransformation					
Biotransformation in aerobic water systems (20°C)	[^{14}C]-triazole labelled flutriafol (99.7%)	Stream water-sand sediment (Virginia Water)	Water: DT_{50}: 27 d; DT_{90}: 91 d (SFO)		2115587, 2115586
			Sediment: Not determined		
			Total system:	Persistent	

Study type	Test material	Value		Comments	PMRA#
			DT$_{50}$: 597 d; DT$_{90}$: 1983 d (SFO)		
		River water-silt loam sediment (Old Basing)	Water: DT$_{50}$: 27 d; DT$_{90}$: 89 d (SFO)		2115587, 2115586
			Sediment: Not determined		
			Total system: DT$_{50}$: 3029 d; DT$_{90}$: 10063 d (SFO)	Persistent	
Biotransformation in anaerobic water systems (25°C)	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (≥98.8%)	Pond water-sandy clay loam sediment	Water: not determined		2115588
			Sediment: not determined		
			Total system: 2809 d; DT$_{90}$: 9331 d (SFO)	Persistent	
Bioconcentration/Bioaccumulation					
Bioconcentration in fish	[^{14}C]-triazole and [^{14}C]-carbinol labelled flutriafol (≥98.2%)	Maximum bioconcentration factor (BCF) values whole fish: 7.2 viscera: 12.8 muscle: 4.9		Low potential to bioaccumulate	2115669

Table 10 Maximum concentrations of transformation products in soil and water

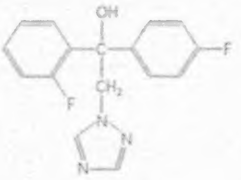
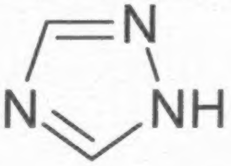
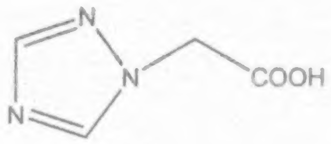
Study	Transformation product	Max % of AR1^{1} (day)	%AR at Study End (study length)
Soil			
Hydrolysis	None		
Phototransformation	1-H triazole	4.1	
	2,4'-difluro-benzophenone	3.6	
Aerobic Biotransformation	None		
Anaerobic Biotransformation	None		
Field dissipation: Europe			

Study	Transformation product	Max % of AR1[1] (day)	%AR at Study End (study length)
Field dissipation: US	Not tracked		
Water			
Hydrolysis			
Phototransformation	5 unidentified	<1.0% except one with 4.1%	
Aerobic Biotransformation	None		
Anaerobic Biotransformation	1,2,4-triazole	Trace (0.1)[2]	0.0 (365)
	1,2,4- triazole-1-analine	Trace (0.5)	0.1 (365)
	1,2,4- triazole-1-acetic acid	Trace (0.3)	0.0 (365)

[1] AR: applied radioactivity

[2] ( ): % of 0-day concentration

Table 11 Structure and properties of parent compound and transformation products

Common name	Chemical name (CAS)	Structure	Formula and molar mass
Flutriafol	(RS)-2,4′-difluoro-α-(1H-1,2,4-triazol-1-ylmethyl)benzhydryl alcohol (IUPAC) α-(2-fluorophenyl)-α-(4-fluorophenyl)-1H-1,2,4-triazole-1-ethanol (CAS)		$C_{16}H_{13}F_2N_3O$ 301.30
1-H triazole	1,2,4-triazole		$C_2H_3N_3$ 69.07
1,2,4-Triazole-1- acetic acid	1H-1,2,4triazol-1-ylacetic acid		$C_4H_5N_3O_2$ 127

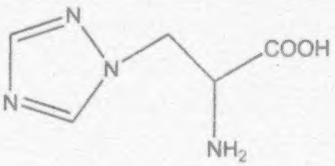
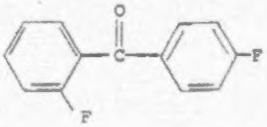
Common name	Chemical name (CAS)	Structure	Formula and molar mass
1,2,4-triazole-1-alanine	3-(1H-1,2,4-triazol-1-yl)-DL-alanine		$C_5H_8N_4O_2$ 156
2,4'-difluorobenzophenone			

Table 12 Screening level EECs in soil and water

Soil[1] (mg a.i./kg soil)	Water[2] (mg a.i./L)	
	15 cm depth	80 cm depth
0.11	0.17 mg a.i./L water	0.032

[1] based on two application of 128 g a.i./ha each with no dissipation between applications (thus the cumulative application rate is 256 g a.i./ha) in the top 15 cm soil depth and a soil bulk density of 1.5 g/cm^3

[2] cumulative application of 256 g a.i./ha based on two application of 128 g a.i./ha each and a total system half-life of 3029 days

Table 13 Level 1 aquatic eco-scenario modelling EECs (µg a.i./L) for 2 applications flutriafol at 128 g a.i./ha, in a water body 0.15 m deep, excluding spray drift

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Strawberries rate: 2 × 128 g a.i./ha at 7-day intervals						
British Columbia	7.3	7.1	6.4	6.3	6.3	6.1
Prairies	184	181	170	167	166	164
Ontario	165	163	157	156	156	153
Quebec	160	158	154	153	152	150
Atlantic	191	188	181	178	177	174

Table 14 Level 1 aquatic eco-scenario modelling EECs (µg a.i./L) for two applications flutriafol at 128 g a.i./ha in a water body 0.80 m deep, excluding spray drift.

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Strawberries rate: 2x 128 g a.i./ha at 7-day intervals						
British Columbia	3.1	3.1	3.1	3.1	3.1	3
Prairies	84	84	83	83	82	82

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Ontario	78	78	78	78	78	77
Quebec	77	76	76	76	76	75
Atlantic	89	89	89	89	88	87

Table 15 EECs in vegetation and insects after a direct over-spray[1]

Food item	EEC (mg a.i./kg fw)[a]		Fresh / dry weight ratios	EEC (mg a.i./kg dw)	
	Maximum Residues	Mean Residues		Maximum Residues	Mean Residues
Short range grass	44.2564	15.7173	3.3[b]	146.0462	51.8669
Leaves and leafy crops	25.0230	8.2721	11[b]	275.2527	90.9926
Long grass	20.2665	6.6176	4.4[b]	89.1726	29.1176
Forage crops	25.0230	8.2721	5.4[b]	135.1241	44.6691
Small insects	10.7537	5.9972	3.8[c]	40.8639	22.7895
Pods with seeds	2.6884	1.2822	3.9[c]	10.4849	5.0005
Large insects	2.6884	1.2822	3.8[c]	10.2160	4.8723
Grain and seeds	2.6884	1.2822	3.8[c]	10.2160	4.8723
Fruit	2.6884	1.2822	7.6[c]	20.4321	9.7445

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973) and modified by Fletcher (1994)

[b] Fresh / dry weight ratios from Harris (1975)

[c] Fresh / dry weight ratios from Spector (1956)

Table 16 Effects of flutriafol on terrestrial organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Invertebrates					
Earthworm (*Eisenia fetida*) Earthworms	14-d Acute	Flutriafol (94.4%)	14-d LC_{50} >1000 mg a.i./kg dry soil	No classification	2149696
	14-d Acute	Flutriafol 125 g/L SC (11.2% flutriafol)	14-d LC_{50} >1000 mg a.i./kg dry soil(32% mortality at 1000 mg a.i./kg dry soil)	No classification	2276666
	56-d Chronic	Flutriafol 125 g/L SC (11.4% flutriafol)	56-d NOEC = 12.167 mg a.i./kg dry soil (reduced number of juveniles)	No classification	2276669
	10-year Field	Flutriafol	10-year NOEC =	No	2276672,

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
	study on permanent grassland	125 g/L SC (12.5% flutriafol)	1 kg a.i./ha/year (highest rate tested)	classification	2276673
Honeybee (*Apis mellifera*)	48-h Oral	Flutriafol (93%)	48-h LD_{50} >2 µg a.i./bee	Not categorized	2115660
	48-h Oral	SC JF 8496 (12.7% flutriafol)	Test 1: 48-h LD_{50} = 47 µg a.i./bee; Test 2: 48-h LD_{50} >50 µg a.i./bee	No classification	2115660
	24-h Oral	IMPACT (12.1% flutriafol)	24-h LD_{50} >198 µg product/bee (>23.9 µg a.i./bee)	No classification	2115661
	48-h Contact	SC JF 8496 (12.7% flutriafol)	Test 1: 48-h LD_{50} >10.5 µg a.i./bee Test 2: 48-h LD_{50} >52.5 µg a.i./bee	Relatively non-toxic	2115660
Predatory mite (*Typhlodromus pyri*)	48-h Contact (glass plate)	CHA 1310-03 (12.5% flutriafol)	48-h LR_{50} = 204.5 g a.i./ha No statistically significant effects on fecundity at 40.2-92.5 g a.i./ha; not evaluated at 213-1125 g a.i./ha	No classification	2276311
Parasitoid wasp (*Aphidius rhopalosiphi*)	48-h Contact (glass plate)	CHA 1310-03 (12.5% flutriafol)	48-h LR_{50} >1125 g a.i./ha Statistically significant reduction in number of aphid mummies/female at all rates tested (23.8 to 44.5% reduction at 13.9 to 1125 g a.i./ha, no dose-response)	No classification	2276310

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
	48-h Contact (barley seedling substrate)	YF7440A (11.7% flutriafol)	48-h LR_{50} >125 g a.i./ha No statistically significant effect on parasitism at 125 g a.i./ha	No classification	2276312
Hoverfly (*Episyrphus balteatus*)	Larvae exposed on bean seedlings until emergence (larvae, food source and test substrate were treated)	YF7440A (11.7% flutriafol)	No statistically significant effect on larval mortality, adult emergence, egg production, egg viability or larva production at 125 g a.i./ha	No classification	2276314
Carabid beetle (*Pterostichus cupreus*)	Adult beetles exposed on soil substrate for 6 days (beetles and soil substrate were treated)	YF7338A (119 g/L flutriafol)	No statistically significant effects on mortality or behaviour at 500 g a.i./ha	No classification	2276315
Wolf spider (*Pardosa* spp.)	Adult spiders exposed on soil substrate for 6 days (spiders and soil substrate were treated)	YF7338A (119 g/L flutriafol)	No statistically significant effects on mortality, behaviour or feeding activity at 500 g a.i./ha	No classification	2276315
Birds					
Bobwhite quail (*Colinus virginianus*)	Acute	Flutriafol (95.1%)	LD_{50} = 810 mg a.i./kg bw	Slightly toxic	2115671
	5-d Dietary	Flutriafol (93%)	5-d LC_{50} = 6532 mg a.i./kg diet; Not converted to an LD_{50} because of food consumption reduction. 5-d NOEC = 2810 mg a.i./kg diet (equivalent	Practically non-toxic	2115674

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
			to NOEL of 396 mg a.i./kg bw/d)		
	22-week Reproduction	Flutriafol (94.4%)	22-w NOEC < 95 mg a.i./kg diet; equivalent to reviewer-calculated NOEL of <10.9 mg a.i./kg bw/d (offspring survival)	No classification	2115676
Mallard duck (*Anas platyrhynchos*)	Acute	Flutriafol (93%)	LD_{50} >5000 mg a.i./kg bw(30% mortality observed at ≥3400 mg a.i./kg bw)	Practically non-toxic	2115672
	5-d Dietary	Flutriafol (93%)	5-d LC_{50} = 3935 mg a.i./kg diet; Not converted to an LD_{50} because of food avoidance. 5-d NOEC = 1832 mg a.i./kg diet (equivalent to NOEL of 346 mg a.i./kg bw/d)	Slightly toxic	2115675
	21-week Reproduction	Flutriafol (95.1%)	21-w NOAEC = 39.2 mg a.i./kg diet (equivalent to NOAEL of 6.0 mg a.i./kg bw/d) (reductions in % hatchlings of 3-week embryos, % of hatchlings of eggs set, 14-d old survivors and number of hatchlings); 21-w LOAEC = 97.5 mg a.i./kg diet (13.1 mg	No classification	2115679

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
			a.i./kg bw/d)		
Red-legged partridge (*Alectoris rufa*)	Acute	Flutriafol (93%)	LD_{50} = 616 mg a.i./kg bw	Slightly toxic	2115673
Tissues of bobwhite quail (*Colinus virginianus*) and mallard duck (*Anas platyrhynchos*)	42-d subchronic (28-d exposure; 24-360 h withdrawal) Accumulation and Depletion via daily gelatin capsules	[^{14}C]-triazole labelled flutriafol (>96%)	The liver was the only tissue with residues equivalent or greater than the daily dose rates. Depletion of residues was rapid upon cessation of dosing.	No classification	2115670
Mammals					
Rat	Acute	Flutriafol (93%)	LD_{50} = 1140 mg/kg bw	Slightly toxic	2115526
	Acute	Fullback 125 SC Fungicide (11.9% flutriafol)	LD_{50} > 2000 mg/kg bw	Practically non-toxic	2115964
	2-Generation dietary reproduction	Flutriafol (93%)	Reproductive and offspring toxicity: NOAEL = 10.2 mg/kg bw/d and LOAEL = 20.8 mg/kg bw/d (increase in pup mortality)	No classification	2115478 2115479
Mouse	Acute	Flutriafol (93%)	LD_{50} = 179 mg/kg bw	Moderately toxic	2115526
Vascular plants					
onion (*Allium cepa*), ryegrass (*Lolium perenne*), wheat (*Triticum aestivum*), corn (*Zea mays*), sugarbeet (*Beta vulgaris*),	21-d Seedling emergence	Flutriafol 125 g/ L SC (11.9% flutriafol)	21-d ER_{25} >134 g a.i./ha	No classification	2115817
	21-d Vegetative vigour (Tier I)	Flutriafol 125 g/ L SC (11.9% flutriafol)	21-d ER_{25} >134 g a.i./ha	No classification	2115818

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
cabbage (*Brassica oleracea*), soybean (*Glycine max*), lettuce (*Lactuca sativa*), tomato (*Lycopersicon esculentum*) and radish (*Raphanus sativus*))					
Ryegrass (*Lolium perenne*)	21-d Vegetative vigour (Tier II)	Flutriafol 125 g/ L SC (11.7% flutriafol)	21-d ER_{25} >268 g a.i./ha	No classification	2115820

[a] Atkins *et al.*(1981) for bees and United States Environmental Protection Agency classification for others, where applicable

Table 17 Effects on aquatic organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Freshwater species					
Water flea (*Daphnia magna*)	48-h Acute	Flutriafol (93%)	48-h EC_{50} = 67 mg a.i./L	Slightly toxic	2115662
	48-h Acute	Flutriafol 125 g/L SC (11.6% flutriafol)	48-h EC_{50} = 7.05 mg product/L (0.83 mg a.i./L)	No classification	2115800
	21-d Chronic	Flutriafol (95.5%)	21-d NOEC = 0.31 mg a.i./L (based on terminal length)	No classification	2115663
	21-d Chronic	Flutriafol (94.4%)	21-d NOEC = 1.0 mg a.i./L (based on reproduction)	No classification	2115664
	21-d Chronic	CHA 1310-03 (12.5% flutriafol)	21-d NOEC = 0.1 mg product/L (0.013 mg	No classification	2115801

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
			a.i./L) (based on survival and reproduction)		
Midge (*Chironomus riparius*)	26-d Chronic, spiked water	Flutriafol (94.4%)	26-d NOEC = 1.6 mg a.i./L (based on development rate)	No classification	2276316
Rainbow trout (*Oncorhynchus mykiss*)	96-h Acute	Flutriafol (93%)	96-h LC_{50} = 61 mg a.i./L	Slightly toxic	2115665
	96-h Acute	Flutriafol 125 g/L SC (11.6% flutriafol)	96-h LC_{50} = 7.9 mg product/L (0.92 mg a.i./L)	No classification	2115808
	28-d Chronic	Flutriafol 125 g/L SC (11.77% flutriafol)	28-d NOEC = 3.3 mg product/L (0.39 mg a.i./L) (based on mortality and sublethal effects)	No classification	2276674
Bluegill sunfish (*Lepomis macrochirus*)	96-h Acute	Flutriafol (93%)	96-h LC_{50} = 33 mg a.i./L	Slightly toxic	2115666
	96-h Acute	Flutriafol (95.1%)	96-h LC_{50} = 46 mg a.i./L	Slightly toxic	2115668
	96-h Acute	Flutriafol 125 g/L SC (11.9% flutriafol)	96-h LC_{50} = 20 mg product/L (2.3 mg a.i./L)	No classification	2115809
Fathead minnow (*Pimephales promelas*)	33-d Early Life Stage (5-d hatching and 28-d post-hatch)	Flutriafol (95.1%)	33-d NOEC = 4.8 mg a.i./L (based on post-hatch survival)	No classification	2276317
Green algae (*Pseudokirchneriella subcapitata*)	96-h Acute	Flutriafol 125 g/L SC (11.9% flutriafol)	96-h EC_{50} (based on biomass) = 5.0 mg product/L (0.60 mg	No classification	2115810

Organism	**Exposure**	**Test substance**	**Endpoint value**	**Degree of toxicity**[a]	**PMRA#**
			a.i./L)		
Green algae (*Selenastrum capricornutum*)	72-hr Acute	Flutriafol 125 g/L SC (12.33% flutriafol)	72-h EC_{50} (based on biomass) = 4.6 mg product/L (0.57 mg a.i./L)	No classification	2276668
Green algae (*Scenedesmus subspicatus*)	72-hr Acute	Flutriafol (94.4%)	72-h EC_{50} (based on biomass) = 1.9 mg a.i./L	No classification	2276321
Diatom (*Navicula pelliculosa*)	96-h Acute	Flutriafol 125 g/L SC (11.9% flutriafol)	96-h EC_{50} (based on biomass) = 1.0 mg a.i./L (estimated to be equivalent to 8.6 mg product/L)	No classification	2288386
Blue-green algae (*Anabaena flos-aquae*)	96-h Acute	Flutriafol 125 g/L SC (11.9% flutriafol)	96-h EC_{50} >121 mg product/L (>14 mg a.i./L)	No classification	2115814
Duckweed (*Lemna gibba*)	7-d Acute (Dissolved)	Flutriafol 125 g/L SC (11.9% flutriafol)	7-d EC_{50} (based on biomass) = 5.6 mg product/L (0.65 mg a.i./L)	No classification	2115822
	7-d Acute (Dissolved)	Flutriafol (95.1%)	7-d EC_{50} (based on yield from frond number) = 1.11 mg a.i./L	No classification	2115821
	7-d Acute (Dissolved)	Flutriafol 125 g/L SC (11.7% flutriafol)	7-d EC_{50} (based on yield from frond number) = 9.8 mg product/L	No classification	2115821

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
			(1.1 mg a.i./L)		
Marine species					
Mysid shrimp (*Americamysis bahia*)	96-h Acute	Flutriafol (95.1%)	96-h LC_{50} = 34.9 mg a.i./L	Slightly toxic	2115802
Eastern oyster (*Crassostrea virginica*)	96-h Acute	Flutriafol (95.1%)	96-h EC_{50} = 25 mg a.i./L	Slightly toxic	2115805
Sheepshead minnow (*Cyprinodon variegatus*)	96-h Acute	Flutriafol (95.1%)	96-h LC_{50} >72.2 mg a.i./L (45% mortality observed at 72.2 mg a.i./L)		2115804
Saltwater diatom (*Skeletonema costatum*)	96-h Acute	Flutriafol 125 g/L SC (11.9% flutriafol)	96-h EC_{50} (based on biomass) = 3.9 mg product/L (0.46 mg a.i./L)	No classification	2115815

[a] United States Environmental Protection Agency classification, where applicable

Table 18 Screening level risk assessment to terrestrial organisms

Organism	Exposure	Endpoint value	EEC	Risk quotient	Risk
Invertebrates					
Earthworm	Acute	(½)LC_{50}: >500 mg a.i./kg soil	0.11 mg a.i./kg soil	<0.001	Negligible
	Chronic	NOEC: 12.167mg a.i./ kg soil	0.11 mg a.i./kg soil	0.01	Negligible
Adult bees	Contact	LD_{50}: > 52.5 µg a.i./bee	0.3072 µg a.i./bee[1]	<0.006	Negligible
	Oral	LD_{50}: 47.0 µg a.i./bee	3.712 µg a.i./bee[2]	0.079	Negligible
	Brood/ hive	Risk from exposure to flutriafol is expected to be low based on the mode of action and low acute toxicity to adult bees.			
Parasitic arthropod (wasp)	Contact, glass plate	LR_{50}: 204.5 g a.i./ha	On-field: 206.80 g a.i./ha[3]	1.01	Negligible
			Off-field (early airblast, 74% drift): 153.03 g a.i./ha	0.75	Negligible

Organism	Exposure	Endpoint value	EEC	Risk quotient	Risk
			Off-field (late airblast, 59% drift): 122.01 g a.i./ha	0.60	Negligible
			Off-field (field sprayer, 6% drift): 12.41 g a.i./ha	0.06	Negligible
Predatory arthropod (mite)	Contact, glass plate	LR_{50}: >1125 g a.i./ha	On-field: 206.80 g a.i./ha[3]	< 0.18	Negligible
			Off-field (early airblast, 74% drift): 153.03g a.i./ha	< 0.14	Negligible
			Off-field (late airblast, 59% drift): 122.01 g a.i./ha	< 0.11	Negligible
			Off-field (field sprayer, 6% drift): 12.41 g a.i./ha	< 0.01	Negligible

[1] contact exposure estimated by multiplying single maximum application rate of 0.128 kg a.i./ha with a factor of 2.4

[2] oral exposure estimated by multiplying single maximum application rate of 0.128 kg a.i./ha with a factor of 29

[3] cumulative application rate calculated using two applications of 128 g a.i./ha at 7-day intervals, and a default foliar DT_{50} of 10 days.

Table 19 Screening level risk assessment for wild birds

	Toxicity (mg a.i/kg bw/d)	Feeding Guild (food item)	EDE (mg a.i/kg bw)	RQ
Small Bird (0.02 kg)				
Acute	61.60	Insectivore (small insects)	10.42	0.17
Reproduction	6.00	Insectivore (small insects)	10.42	1.74
Medium Sized Bird (0.1 kg)				
Acute	61.60	Insectivore (small insects)	8.13	0.13
Reproduction	6.00	Insectivore (small insects)	8.13	1.36
Large Sized Bird (1 kg)				
Acute	61.60	Herbivore (short grass)	8.49	0.14
Reproduction	6.00	Herbivore (short grass)	8.49	1.41

Shaded values indicate that the level of concern is exceeded.

Table 20 Further characterization of reproductive risk to wild birds using screening level endpoints (NOAEL) and percent drift

		On-field				Off field (74% drift)				Off field (59% drift)				Off field (6% drift)			
		Maximum residue		Mean residue		Maximum residues		Mean residues		Maximum residues		Mean residues		Maximum residues		Mean residues	
Toxicity (mg a.i/kg bw/d)	**Food Guild (food item)**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**
Reproductive risk to small sized bird (0.02 kg)																	
6	Insectivore (small insects)	10.42	1.74	5.81	0.97	7.71	1.29	4.3	0.72	6.15	1.02	3.43	0.57	0.63	0.1	0.35	0.06
6	Granivore (grain and seeds)	2.61	0.43	1.24	0.21	1.93	0.32	0.92	0.15	1.54	0.26	0.73	0.12	0.16	0.03	0.07	0.01
6	Frugivore (fruit)	5.21	0.87	2.48	0.41	3.86	0.64	1.84	0.31	3.07	0.51	1.47	0.24	0.31	0.05	0.15	0.02
Reproductive risk to medium sized bird (0.1 kg)																	
6	Insectivore (small insects)	8.13	1.36	4.54	0.76	6.02	1.00	3.36	0.56	4.8	0.8	2.68	0.45	0.49	0.08	0.27	0.05
6	Insectivore (large insects)	2.03	0.34	0.97	0.16	1.5	0.25	0.72	0.12	1.2	0.2	0.57	0.1	0.12	0.02	0.06	0.01
6	Granivore (grain and seeds)	2.03	0.34	0.97	0.16	1.5	0.25	0.72	0.12	1.2	0.2	0.57	0.1	0.12	0.02	0.06	0.01
6	Frugivore (fruit)	4.07	0.68	1.94	0.32	3.01	0.5	1.43	0.24	2.4	0.4	1.14	0.19	0.24	0.04	0.12	0.02
Reproductive risk to large sized bird (1 kg)																	
6	Insectivore (small insects)	2.37	0.4	1.32	0.22	1.76	0.29	0.98	0.16	1.4	0.23	0.78	0.13	0.14	0.02	0.08	0.01
6	Insectivore (large insects)	0.59	0.1	0.28	0.05	0.44	0.07	0.21	0.03	0.35	0.06	0.17	0.03	0.04	0.01	0.02	0
6	Granivore (grain and seeds)	0.59	0.1	0.28	0.05	0.44	0.07	0.21	0.03	0.35	0.06	0.17	0.03	0.04	0.01	0.02	0
6	Frugivore (fruit)	1.19	0.2	0.57	0.09	0.88	0.15	0.42	0.07	0.7	0.12	0.33	0.06	0.07	0.01	0.03	0.01
6	Herbivore (short grass)	8.49	1.41	3.01	0.5	6.28	1.05	2.23	0.37	5.01	0.83	1.78	0.3	0.51	0.08	0.18	0.03

		On-field				Off field (74% drift)				Off field (59% drift)				Off field (6% drift)			
		Maximum residue		Mean residue		Maximum residues		Mean residues		Maximum residues		Mean residues		Maximum residues		Mean residues	
Toxicity (mg a.i/kg bw/d)	**Food Guild (food item)**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**
6	Herbivore (long grass)	5.18	0.86	1.69	0.28	3.83	0.64	1.25	0.21	3.06	0.51	1	0.17	0.31	0.05	0.1	0.02
6	Herbivore (forage crops)	7.85	1.31	2.6	0.43	5.81	0.97	1.92	0.32	4.63	0.77	1.53	0.26	0.47	0.08	0.16	0.03

[1]The percent drift for airblast application was considered as a conservative approach in this assessment, because the highest cumulative rate used in the assessment is for use on strawberries, which would not involve airblast application equipment. Other proposed uses of flutriafol on grapes and apples involve airblast application, but the cumulative rate of application is slightly lower; Shaded values indicate that the level of concern is exceeded.

Table 21 Further characterization of reproductive risk to wild birds using the lowest observable adverse effect level (LOAEL)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field (74% drift)		On-field		Off Field (74% drift)	
	Toxicity (mg a.i/kg bw/d)	**Food Guild (food item)**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**
Small Bird (0.02 kg)										
Reproduction	13.10	Insectivore (small insects)	10.42	0.80	7.71	0.59	5.81	0.44	4.30	0.33
	13.10	Granivore (grain and seeds)	2.61	0.20	1.93	0.15	1.24	0.09	0.92	0.07
	13.10	Frugivore (fruit)	5.21	0.40	3.86	0.29	2.48	0.19	1.84	0.14
Medium Sized Bird (0.1 kg)										
Reproduction	13.10	Insectivore (small insects)	8.13	0.62	6.02	0.46	4.54	0.35	3.36	0.26
	13.10	Insectivore (large insects)	2.03	0.16	1.50	0.11	0.97	0.07	0.72	0.05
	13.10	Granivore (grain and seeds)	2.03	0.16	1.50	0.11	0.97	0.07	0.72	0.05
	13.10	Frugivore (fruit)	4.07	0.31	3.01	0.23	1.94	0.15	1.43	0.11

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field (74% drift)		On-field		Off Field (74% drift)	
	Toxicity (mg a.i/kg bw/d)	Food Guild (food item)	EDE (mg a.i/kg bw)	RQ	EDE (mg a.i/kg bw)	RQ	EDE (mg a.i/kg bw)	RQ	EDE (mg a.i/kg bw)	RQ
Large Sized Bird (1 kg)										
Reproduction	13.10	Insectivore (small insects)	2.37	0.18	1.76	0.13	1.32	0.10	0.98	0.07
	13.10	Insectivore (large insects)	0.59	0.05	0.44	0.03	0.28	0.02	0.21	0.02
	13.10	Granivore (grain and seeds)	0.59	0.05	0.44	0.03	0.28	0.02	0.21	0.02
	13.10	Frugivore (fruit)	1.19	0.09	0.88	0.07	0.57	0.04	0.42	0.03
	13.10	Herbivore (short grass)	8.49	0.65	6.28	0.48	3.01	0.23	2.23	0.17
	13.10	Herbivore (long grass)	5.18	0.40	3.83	0.29	1.69	0.13	1.25	0.10
	13.10	Herbivore (forage crops)	7.85	0.60	5.81	0.44	2.60	0.20	1.92	0.15

Table 22 Screening level risk assessment for wild mammals

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Mammal (0.015 kg)				
Acute	17.90	Insectivore (small insects)	5.99	0.33
Reproduction	10.20	Insectivore (small insects)	5.99	0.59
Medium Sized Mammal (0.035 kg)				
Acute	17.90	Herbivore (short grass)	18.78	1.05
Reproduction	10.20	Herbivore (short grass)	18.78	1.84
Large Sized Mammal (1 kg)				
Acute	17.90	Herbivore (short grass)	10.03	0.56
Reproduction	10.20	Herbivore (short grass)	10.03	0.98

Shaded values indicate that the level of concern is exceeded.

Table 23 Further characterization of risk to wild mammals using screening level endpoints (NOAEL) and percent drift

			On-field				Off field (74% drift)				Off Field (59% drift)				Off Field (6% drift)			
			Maximum residues		Mean residues		Maximum residues		Mean residues		Maximum residues		Mean residues		Maximum residues		Mean residues	
	Toxicity (mg a.i/kg bw/d)	**Food Guild (food item)**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**	**EDE (mg a.i/kg bw)**	**RQ**
Medium Sized Mammal (0.035 kg)																		
Acute	17.9	Insectivore (small insects)	5.25	0.29	2.93	0.16	3.89	0.22	2.17	0.12	3.1	0.17	1.73	0.1	0.32	0.02	0.18	0.01
	17.9	Insectivore (large insects)	1.31	0.07	0.63	0.03	0.97	0.05	0.46	0.03	0.77	0.04	0.37	0.02	0.08	0	0.04	0
	17.9	Granivore (grain and seeds)	1.31	0.07	0.63	0.03	0.97	0.05	0.46	0.03	0.77	0.04	0.37	0.02	0.08	0	0.04	0
	17.9	Frugivore (fruit)	2.63	0.15	1.25	0.07	1.94	0.11	0.93	0.05	1.55	0.09	0.74	0.04	0.16	0.01	0.08	0
	17.9	Herbivore (short grass)	18.78	1.05	6.67	0.37	13.9	0.78	4.93	0.28	11.08	0.62	3.93	0.22	1.13	0.06	0.4	0.02
	17.9	Herbivore (long grass)	11.47	0.64	3.74	0.21	8.48	0.47	2.77	0.15	6.76	0.38	2.21	0.12	0.69	0.04	0.22	0.01
	17.9	Herbivore (forage crops)	17.37	0.97	5.74	0.32	12.86	0.72	4.25	0.24	10.25	0.57	3.39	0.19	1.04	0.06	0.34	0.02
Reproduction	10.2	Insectivore (small insects)	5.25	0.52	2.93	0.29	3.89	0.38	2.17	0.21	3.1	0.3	1.73	0.17	0.32	0.03	0.18	0.02
	10.2	Insectivore (large insects)	1.31	0.13	0.63	0.06	0.97	0.1	0.46	0.05	0.77	0.08	0.37	0.04	0.08	0.01	0.04	0
	10.2	Granivore (grain and seeds)	1.31	0.13	0.63	0.06	0.97	0.1	0.46	0.05	0.77	0.08	0.37	0.04	0.08	0.01	0.04	0
	10.2	Frugivore (fruit)	2.63	0.26	1.25	0.12	1.94	0.19	0.93	0.09	1.55	0.15	0.74	0.07	0.16	0.02	0.08	0.01
	10.2	Herbivore (short grass)	18.78	1.84	6.67	0.65	13.9	1.36	4.93	0.48	11.08	1.09	3.93	0.39	1.13	0.11	0.4	0.04
	10.2	Herbivore (long grass)	11.47	1.12	3.74	0.37	8.48	0.83	2.77	0.27	6.76	0.66	2.21	0.22	0.69	0.07	0.22	0.02
	10.2	Herbivore (forage crops)	17.37	1.7	5.74	0.56	12.86	1.26	4.25	0.42	10.25	1.00	3.39	0.33	1.04	0.1	0.34	0.03

[1] The percent drift for early airblast application was considered as a conservative approach in this assessment, because the highest cumulative rate used in the assessment is for use on strawberries, which would not involve airblast application equipment. Other

proposed uses of flutriafol on grapes and apples involve airblast application, but the cumulative rate of application is slightly lower. Shaded values indicate that the level of concern is exceeded.

Table 24 Refined assessment of reproductive risk to mammals using the lowest observed adverse effect level (LOAEL)

			Maximum nomogram residues				**Mean nomogram residues**			
			On-field		**Off Field (74% drift)**		**On-field**		**Off Field (74% drift)**	
	Toxicity (mg a.i/kg bw/d)	**Food Guild (food item)**	**EDE (mg a.i/.kg bw)**	**RQ**	**EDE (mg a.i./kg bw)**	**RQ**	**EDE (mg a.i./kg bw)**	**RQ**	**EDE (mg a.i./kg bw)**	**RQ**
Medium Sized Mammal (0.035 kg)										
Reproduction	20.80	Insectivore (small insects)	5.25	0.25	3.89	0.19	2.93	0.14	2.17	0.10
	20.80	Insectivore (large insects)	1.31	0.06	0.97	0.05	0.63	0.03	0.46	0.02
	20.80	Granivore (grain and seeds)	1.31	0.06	0.97	0.05	0.63	0.03	0.46	0.02
	20.80	Frugivore (fruit)	2.63	0.13	1.94	0.09	1.25	0.06	0.93	0.04
	20.80	Herbivore (short grass)	18.78	0.90	13.90	0.67	6.67	0.32	4.93	0.24
	20.80	Herbivore (long grass)	11.47	0.55	8.48	0.41	3.74	0.18	2.77	0.13
	20.80	Herbivore (forage crops)	17.37	0.84	12.86	0.62	5.74	0.28	4.25	0.20

[1] The percent drift for early airblast application was considered as a conservative approach in this assessment, because the highest cumulative rate used in the assessment is for use on strawberries, which would not involve airblast application equipment. Other proposed uses of flutriafol on grapes and apples involve airblast application, but the cumulative rate of application is slightly lower.

Table 25 Screening level risk assessment for terrestrial plants

Organism	Exposure	Endpoint value	EEC	RQ	Risk
Vascular plant	Seedling emergence	ER$_{25}$: >134 g a.i./ha	256 g a.i./ha^{1}	<1.91	Exceeds LOC
	Vegetative vigour	ER$_{25}$: >268 g a.i./ha	206.80g a.i./ha^{2}	<0.77	Negligible

^{1}maximum cumulative application rate

^{2}cumulative application rate with default foliar half-life of 10 days

Table 26 Refined risk assessment for terrestrial plants based on a cumulative application rate of 256 g a.i./ha for seedling emergence (as proposed for strawberries)

	Airblast early (74% drift)	Airblast late (59% drift)	Ground boom (6% drift)
Seedling emergence (two applications of 128 g a.i./ha each)			
Cumulative application rate (2 applications at a 7-day interval adjusted for % drift)	189.44 g a.i./ha	151.04 g a.i./ha	15.36g a.i./ha
RQ with EC$_{25}$ of >134 g a.i./ha for seedling emergence	<1.40	<1.13	<0.11

Table 27 Screening level risk assessment to aquatic organisms

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	Risk
Freshwater species					
Daphnia magna	Acute (end-use product)	48-h LC$_{50}$(1/2):0.415	0.032*	0.08	Negligible
	Chronic	21-d NOEC: 0.013	0.032*	2.46	Exceeds LOC
Rainbow trout	Acute (end-use product)	96-h LC$_{50}$(1/10): 0.092	0.032*	0.35	Negligible
	Chronic (end-use product)	28-d NOEC:0.39	0.032*	0.08	Negligible
Bluegill sunfish	Acute (end-use product)	96-h LC$_{50}$(1/10): 0.23	0.032*	0.14	Negligible
Fathead minnow	Early-life stage	33-d NOEC: 4.8	0.032*	0.01	Negligible
Amphibians	Acute (end-use product)	Fish 96-h LC$_{50}$(1/10): 0.092	0.17**	1.85	Exceeds LOC
	Chronic (end-use	Fish 28-d NOEC: 0.39	0.17**	0.44	Negligible

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	Risk
	product)				
Freshwater midge (*C. riparius*)	Chronic	26-d NOEC: 1.6	0.032*	0.02	Negligible
Freshwater algae (green algae)	Acute (end-use product)	72-h EC_{50} (1/2): 0.285	0.032*	0.11	Negligible
Vascular plants (duck weed)	Acute (end-use product)	7-d EC_{50} (1/2):0.325	0.032*	0.10	Negligible
Marine species					
Crustacean (Eastern Oyster)	Acute	96-h LC_{50} (1/2): 12.5	0.032*	0.002	Negligible
Saltwater fish (sheepshead minnow)	Acute	96-h LC_{50} (1/10): >7.22	0.032*	<0.004	Negligible
Saltwater diatom (*S. costatum*)	Acute	96-h EC_{50} (1/2):0.23	0.032*	0.14	Negligible

* 80 cm water depth

**15 cm water depth

Table 28 Screening level risk to aquatic organisms from runoff

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	Risk
Freshwater species					
Daphnia magna	Acute	48-h LC_{50}(1/2): 0.415	0.089*	0.21	Negligible
	Chronic	21-d NOEC: 0.013	0.089*	6.85	Exceeds LOC
Rainbow trout	Acute	96-h LC_{50}(1/10): 0.092	0.089*	0.97	Negligible
	Chronic	28-d NOEC: 0.39	0.089*	0.23	Negligible
Bluegill sunfish	Acute	96-h LC_{50}(1/10): 0.23	0.089*	0.39	Negligible
Fathead minnow	Early life stage	33-d NOEC: 4.8	0.089*	0.02	Negligible
Amphibians	Acute	Fish 96-h LC_{50}(1/10): 0.092	0.191*	2.08	Exceeds LOC
	Chronic	Fish 28-d NOEC: 0.39	0.181*	0.46	Negligible
Freshwater midge (*C. riparius*)	Chronic	26-d NOEC: 1.6	0.089*	0.06	Negligible
Freshwater algae (green algae)	Acute	72-h EC_{50} (1/2): 0.285	0.089*	0.31	Negligible
Vascular plants (duck weed)	Acute	7-d EC_{50} (1/2): 0.325	0.089*	0.27	Negligible
Marine species					
Crustacean	Acute	96-h LC_{50} (1/2): 12.5	0.089*	0.01	Negligible

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	Risk
(Eastern Oyster)					
Saltwater fish (sheepshead minnow)	Acute	96-h LC_{50} (1/10): >7.22	0.089*	< 0.01	Negligible
Saltwater diatom (*S. costatum*)	Acute	96-h EC_{50} (1/2): 0.23	0.089*	0.39	Negligible

* 80 cm water depth; **15 cm water depth

Table 29 Refined risk assessment to *Daphnia* sp and amphibians: Spray drift

	Airblast early (74% drift)	Airblast late (59% drift)	Ground boom (6% drift)
Application rate (128 g a.i./ha)	94.72 g a.i./ha	75.52 g a.i./ha	7.68 g a.i/ha
Cumulative application rate (2 applications, 7 d interval, DT_{50} of 3029 days)	189.288g a.i./ha	150.919 g a.i./ha	15.348 g a.i./ha
EEC (80 cm depth for *Daphnia* and fish)	0.024 mg a.i./L	0.019 mg a.i./L	0.002 mg a.i./L
EEC (15 cm depth for amphibians)	0.126 mg a.i./L	0.100 mg a.i./L	0.010 mg a.i./L
Fish: Acute risk RQ (1/10 LC_{50}: 0.092 mg a.i./L)	0.26	0.20	0.022
Amphibians: Acute RQ(1/10 LC_{50}: 0.092 mg a.i./L)	1.37	1.09	0.11
Daphnia sp: Chronic RQ (NOEC: 0.013 mg a.i./L)	1.85	1.46	0.15

Table 30 Buffer zones for aquatic and terrestrial habitat

Method of application	Crop		Buffer Zones (meters) required for the protection of:		
			Aquatic habitat of depths:		Terrestrial habitat
			Less than 1 m	Greater than 1 m	
Field sprayer	Strawberries, soybeans		1	0	1
Airblast	Apples, grapes	Early growth stage	2	0	2
		Late growth stage	1	0	1

Table 31 Label statements

Label statements
Toxic to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE. Flutriafol is persistent and may carryover. It is recommended that any products containing flutriafol not be used in areas treated with this product during the previous season. This product demonstrates the properties and characteristics associated with chemicals detected in ground water. The use of flutriafol in areas where soils are permeable, particularly where the water table is shallow, may result in ground water contamination. To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay. Avoid application when heavy rain is forecast. Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body

Table 32 TSMP considerations-comparison to TSMP Track 1 criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Flutriafol Endpoints	Comments
Toxic or toxic-equivalent as defined by the *Canadian Environmental Protection Act*[1]	Yes		Yes	
Predominantly anthropogenic[2]	Yes		Yes	
Persistence[3]	Soil	Half-life ≥ 182 days	811-4807 days (laboratory); 318-615 days (field, cropped plots); 195-437 days (field, bareground plots)	
	Water	Half-life ≥ 182 days	Half-life: 27 days	
	Sediment	Half-life ≥ 365 days	Total system half-life: 597 to 3029 days	
	Air	Half-life ≥ 2 days or evidence of long range transport	Physico-chemical properties of flutriafol indicate a low potential for volatilization; however, residues of flutriafol were detected in Norwegian arctic ice core and in surface water and groundwater in British Columbia and Ontario although the product is not used in Canada. Therefore, flutriafol is considered as having a potential for long range	

TSMP Track 1 Criteria	**TSMP Track 1 Criterion value**	**Flutriafol Endpoints**	**Comments**
		transport	
Bioaccumulation[4]	$\log K_{OW} \geq 5$	2.3	
	$BCF \geq 5000$	7.2	
	$BAF \geq 5000$	not available	
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?		No, does not meet TSMP Track 1 criteria.	

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[1] All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).

[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

[4] Field data (for example, bioaccumulation factors [BAFs]) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{OW}).

Table 33 Registered alternative products for the crops and pests to be registered on the Fullback 125 SC Fungicide label as of 22 May 2014

Crop	**Disease**	**Active Ingredient (Mode of Action Group)**
Grape	Powdery mildew (*Erysiphe necator* syn. *Uncinula necator*)	sulphur (M) copper (M) myclobutanil (3) tetraconazole (3) difenoconazole (3) boscalid (7) fluopyram + pyrimethanil (7+9) kresoxim-methyl (11) trifloxystrobin (11) quinoxyfen (13) *Bacillus subtilis* (44) metrafenone (U8) mineral oil (NC) potassium bicarbonate (NC) *Streptomyces lydicus* (NC) extract of *Reynoutria sachalinensis* (NC) garlic powder (NC) tea tree oil (NC)

Crop	**Disease**	**Active Ingredient (Mode of Action Group)**
Apple	Scab (*Venturia inaequalis*)	sulphur (M) captan (M) mancozeb (M) ziram (M) folpet (M) chlorothalonil (M) metiram (M) ferbam (M) thiram (M) dodine (U12) thiophanate-methyl (1) myclobutanil (3) flusilazole (3) difenoconazole (3) penthiopyrad (7) fluopyram (7) fluxapyroxad (7) cyprodinil (9) pyrimethanil (9) kresoxim-methyl (11) trifloxystrobin (11) boscalid + pyraclostrobin (7+11) fluazinam (29) *Bacillus subtilis* (44) garlic powder (NC)
	Powdery mildew (*Podosphaera leucotricha*)	sulphur (M) thiophanate-methyl (1) myclobutanil (3) flusilazole (3) triforine (3) difenoconazole (3) penthiopyrad (7) fluxapyroxad (7) fluopyram + pyrimethanil (7+9) boscalid + pyraclostrobin (7+11) cyprodinil (9) kresoxim-methyl (11) trifloxystrobin (11) *Bacillus subtilis* (44) mineral oil (NC)
	Cedar-apple rust (*Gymnosporangium juniper-virginianae*)	chlorothalonil (M) metiram (M) ferbam (M) mancozeb (M) thiram (M)

Crop	**Disease**	**Active Ingredient (Mode of Action Group)**
		difenoconazole (3) penthiopyrad (7) trifloxystrobin (11)
	Quince rust (*Gymnosporangium clavipes*)	mancozeb (M) metiram (M) ferbam (M) difenoconazole (3)
Strawberry	Powdery mildew (*Sphaerotheca aphanis* syn. *S. macularis*)	sulphur (M) tetraconazole (3) fluopyram (7) boscalid + pyraclostrobin (7+11) trifloxystrobin (11) quinoxyfen (13) *Streptomyces lydicus* (NC) lactic acid + citric acid (NC) extract of *Reynoutria sachalinensis* (NC) tea tree oil (NC)
Soybean	Asian soybean rust (*Phakopsora pachyrhizi*)	propiconazole (3) tebuconazole (3) prothioconazole (3) metconazole (3) propiconazole + azoxystrobin (3+11) propiconazole + trifloxystrobin (3+11) tebuconazole + trifloxystrobin (3+11) penthiopyrad (7) fluxapyroxad (7) fluxapyroxad + pyraclostrobin (7+11) azoxystrobin (11) pyraclostrobin (11)
	Frogeye leaf spot (*Cercospora sojina*)	propiconazole (3) tebuconazole (3) prothioconazole (3) tebuconazole + trifloxystrobin (3+11) propiconazole + azoxystrobin (3+11) propiconazole + trifloxystrobin (3+11) penthiopyrad (7) fluxapyroxad (7) fluxapyroxad + pyraclostrobin (7+11) pyraclostrobin (11) fluoxastrobin (11) picoxystrobin (11) *Bacillus subtilis* (44)
	Cercospora leaf spot (*Cercospora kikuchii*)	propiconazole (3) azoxystrobin (11)
	Brown spot (*Septoria glycines*)	penthiopyrad (7)

Crop	Disease	Active Ingredient (Mode of Action Group)
		fluxapyroxad (7) fluxapyroxad + pyraclostrobin (7+11) picoxystrobin (11) *Bacillus subtilis* (44)

Table 34 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Use claim	Supported / Not Supported
To control scab (*Venturia inaequalis*) on apple, apply Fullback 125 SC Fungicide at 950 ml/ha (119 g a.i./ha) or 25 ml/100L water (3.1 g a.i./100L) between green tip and cover sprays. Initiate applications at green tip or when environmental conditions are favorable for primary scab development. Applications should continue through the duration of primary scab. Observed spray intervals of 7-10 days through petal fall and 10-14 days after petal fall. It is recommended that Fullback 125 SC Fungicide be tank-mixed with a protectant fungicide at labeled rates for apple scab resistant management. Do not apply more than 3.8 L/ha/season. Do not apply more than 4 applications per growing season.	Supported at proposed rates and timings. The maximum seasonal application rate is amended to **2048 ml/ha/season**. The number of applications per season should not exceed two based on the application rate. The tank mix statement will be amended to recommend Dithane DG 75 Fungicide as a tank mix partner.
To control powdery mildew (*Podosphaera leucotricha*) on apple, apply Fullback 125 SC Fungicide at 585 - 877 ml/ha (73 - 110 g a.i./ha) or 15.6–23.4 ml/100L water (2 - 3 g a.i./100L). Initiate applications at green tip and continue on 10–14 day intervals through cover sprays. Do not apply more than 3.8 L/ha/season. Do not apply more than 4 applications per growing season.	Supported at proposed rates and timings. The maximum seasonal application rate is amended to **2048 ml/ha/season**. The number of applications per season will be dependent on rates applied.
To control cedar-apple rust (*Gymnosporangium juniperi-virginianae*) on apple, apply Fullback 125 SC Fungicide at 585 - 877 ml/ha (73 - 110 g a.i./ha) or 15.6–23.4 ml/100L water (2 - 3 g a.i./100L). Initiate applications at green tip and continue on 10–14 day intervals through cover sprays. Do not apply more than 3.8 L/ha/season. Do not apply more than 4 applications per growing season.	Supported at proposed rates and timings. The maximum seasonal application rate is amended to **2048 ml/ha/season**. The number of applications per season will be dependent on rates applied.

Use claim	Supported / Not Supported
To control quince rust (*Gymnosporangium clavipes*) on apple, apply Fullback 125 SC Fungicide at 585 - 877 ml/ha (73 - 110 g a.i./ha) or 15.6–23.4 ml/100L water (2 - 3 g a.i./100L). Initiate applications at green tip and continue on 10–14 day intervals through cover sprays. Do not apply more than 3.8 L/ha/season. Do not apply more than 4 applications per growing season.	Supported at proposed rates and timings. The maximum seasonal application rate is amended to **2048 ml/ha/season**. The number of applications per season will be dependent on rates applied.
To control powdery mildew (*Erysiphe necator* syn. *Uncinula necator*) on grapes, apply Fullback 125 SC Fungicide at 585 - 731 ml/ha (73 - 91 g a.i./ha) on a 14–21 day interval. Apply as a foliar spray beginning at 15–25 cm shoots. Use the higher rate and/or shorter intervals when disease pressure is high. Apply in sufficient water for thorough coverage of vines and fruit. Do not apply more than 6 applications per growing season. Do not apply more than 4.4 liters per hectare per season.	Supported at proposed rates and timings. The maximum seasonal application rate is amended to **2048 ml/ha/season**. The number of applications per season will be dependent on rates applied.
To control powdery mildew (*Sphaerotheca aphanis* syn. *Sphaerotheca macularis*) on strawberry, apply Fullback 125 SC Fungicide at 512–1024 ml/ha (64–128 g a.i./ha) on a 7–10 day interval. Begin applications when conditions are favourable for disease development. Use the higher rate and/or shorter spray interval under severe sustained disease pressure. A non-ionic surfactant at 0.25% v/v may be added to the spray solution. Do not apply more than 4 applications per growing season.	Supported at proposed rates and timings. The maximum seasonal application rate is limited to **2048 ml/ha/season**. The number of applications per season will be dependent on rates applied.
To control Asian soybean rust (*Phakopsora pachyrhizi*) on soybean, apply Fullback 125 SC as a broadcast foliar spray at a rate of 512–1024 ml/ha (64–128 g a.i./ha) when conditions are favourable for development of soybean rust. Repeat after first application if environmental conditions are favourable for continued disease development on a 21–35 day intervals. Apply in a minimum of 100 L of spray solution per hectare by ground sprayer. Fullback 125 SC may be tank mixed with other approved fungicides, herbicides, or insecticides unless prohibited on the label. Do not apply more than 3 applications per growing season.	Supported as proposed. **The maximum seasonal application rate will be expressed as 2048 ml/ha/season to be consistent with the rest of the label.** The tank mix statement will be amended to recommend Headline EC Fungicide as a tank mix partner.

Use claim	Supported / Not Supported
Do not apply more than 2.05 liters per hectare per season. Only one application at 1024 ml/ha may be made to any one field during a single growing season.	
To control frogeye leaf spot (*Cercospora sojina*) on soybean, apply Fullback 125 SC as a broadcast foliar spray at rates of 512–1024 ml/ha (64–128 g a.i./ha) to soybean plants in R3 growth stage (early pod fill) or when environmental conditions are favourable for disease development. Apply second application on a 14–21 day interval if conditions are conducive for heavy disease development. Use the higher rate and shorter spray interval under severe sustained disease pressure. Do not apply more than 3 applications per growing season. Do not apply more than 2.05 liters per hectare per season. Only one application at 1024 ml/ha may be made to any one field during a single growing season.	Supported as **suppression** at the proposed rates and timings. **The maximum seasonal application rate will be expressed as 2048 ml/ha/season to be consistent with the rest of the label.**
To control brown spot (*Septoria glycines*) on soybean, apply Fullback 125 SC as a broadcast foliar spray at rates of 512–1024 ml/ha (64–128 g a.i./ha) to soybean plants in R3 growth stage (early pod fill) or when environmental conditions are favourable for disease development. Apply second application on a 14–21 day interval if conditions are conducive for heavy disease development. Use the higher rate and shorter spray interval under severe sustained disease pressure. Do not apply more than 3 applications per growing season. Do not apply more than 2.05 liters per hectare per season. Only one application at 1024 ml/ha may be made to any one field during a single growing season.	Supported as **suppression** at the proposed rates and timings. **The maximum seasonal application rate will be expressed as 2048 ml/ha/season to be consistent with the rest of the label.**
To control cercospora blight and leaf spot (*Cercospora kikuchii*) on soybean, apply Fullback 125 SC as a broadcast foliar spray at rates of 512–1024 ml/ha (64–128 g a.i./ha) to soybean plants in R3 growth stage (early pod fill) or when environmental conditions are favourable for disease development. Apply second application on a 14–21 day interval if conditions are conducive for heavy disease development. Use the higher rate and shorter	Supported as **suppression** at the proposed rates and timings. **The maximum seasonal application rate will be expressed as 2048 ml/ha/season to be consistent with the rest of the label.**

Use claim	Supported / Not Supported
spray interval under severe sustained disease pressure. Do not apply more than 3 applications per growing season. Do not apply more than 2.05 liters per hectare per season. Only one application at 1024 ml/ha may be made to any one field during a single growing season.	

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Flutriafol is a new active ingredient which is being registered in Canada. The MRLs proposed for flutriafol in Canada are the same as corresponding tolerances established in the United States (except for peanuts, dry soybeans, and livestock commodities), in accordance with Table 1.

Table 1 compares the MRLs proposed for flutriafol in Canada with corresponding American tolerances and Codex MRLs[9]. American tolerances are listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide. A listing of established Codex MRLs is available on the Codex Alimentarius Pesticide Residues in Food website, by pesticide or commodity.

Table 1 Comparison of Canadian MRLs, American Tolerances and Codex MRLs

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)	Codex MRL (ppm)
Raisins	2.4	2.4	2.0
Stone fruits (Crop Group 12-09)	1.5	1.5	None
Small fruit vine climbing, except fuzzy kiwifruit (Crop Subgroup 13-07F)	1.5	1.5	0.8 (grapes)
Low growing berry (Crop Subgroup 13-07G)	1.5	1.5	None
Pome fruits (Crop Group 11-09)	0.4	0.4	0.3
Dry soybeans	0.4	0.35	0.4
Bananas	0.3	0.3	0.3
Peanuts	0.15	0.09	0.15
Sugar beet roots	0.08	0.08	None
Corn oil (refined)	0.02	0.02	None
Meat byproducts of cattle, goats, horses, and sheep	0.015	0.05 (except liver at 0.8)	None
Eggs	0.01	None	None
Fat of cattle, goats, hogs, horses, poultry, and sheep	0.01	0.05 (except fat of hogs at 0.01, and none for fat of poultry)	None
Field corn grain, popcorn grain	0.01	0.01	None
Meat byproducts of hogs	0.01	0.01	None
Meat byproducts of poultry	0.01	None	None
Meat of cattle, goats, hogs, horses, poultry, and sheep	0.01	0.01 (except meat of poultry)	None
Milk	0.01	0.01	None

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

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[9] The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

Under the North American Free Trade Agreement (NAFTA), Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
2115555	Validation of Analytical Method VAM 022-02 for determination of [CBI removed] in technical pesticide or its formulations, DACO: 2.13.1 CBI
2115556	Validation of analytical method VAM 083-02 for determination of Flutraifol (CAS No. 76674-21-0) in Flutriafol technical and Flutriafol SC-formulation, DACO: 2.13.1 CBI
2115557	Validation of analytical method VAM 103-01 for determination of REF 192 in Flutriafol Technical and SC formulation, DACO: 2.13.1 CBI
2115558	Validation of analytical method VAM 104-01 for determination of REF 190 in Flutriafol Technical, DACO: 2.13.1 CBI
2115559	Validation of analytical method VAM 105-01 for determination of REF 170, REF 187, REF 188, REF 189, REF 191 and REF 290 in Flutriafol Technical, DACO: 2.13.1 CBI
2115561	Validation of analytical method VAM 106-01 for determination of REF 169 and CER 202 in Flutriafol Technical, DACO: 2.13.1 CBI
2115563	Validation of analytical method VAM 107-01 for determination of REF 090, REF 291 and REF 292 in Flutriafol Technical, DACO: 2.13.1 CBI
2115564	Analytical Method VAM 022-02, Determination of water in technical pesticide or its formulations, DACO: 2.13.1 CBI
2115565	Analytical Method VAM 083-02, Determination of Flutrifol (CAS No. 76674-21-0) in Flutrifol technical and SC formulations, DACO: 2.13.1 CBI
2115566	Analytical Method VAM 103-01, Determination of REF 192 in Flutrifol technical and SC formulations, DACO: 2.13.1 CBI
2115567	Analytical Method VAM 104-01, Determination of REF 190 in Flutrifol technical, DACO: 2.13.1 CBI
2115569	Analytical Method VAM 105-01, Determination of REF 170, REF 187, REF 188, REF 189 and REF 191 in Flutrifol technical, DACO: 2.13.1 CBI
2115570	Analytical Method VAM 106-01, Determination of REF 169 and CER 202 in Flutrifol technical, DACO: 2.13.1 CBI
2115571	Analytical Method VAM 107-01, Determination of REF 090, REF 291 and REF 292 in Flutrifol technical, DACO: 2.13.1 CBI

2115572	Identification and determination of active ingredinet Flutriafol (CAS No.76674-21-0) and impurities in five samples of Flutriafol Technical (wet paste), Batch Nos.: 1673, 1674, 1570/3, 1581/3 and 1584/1, DACO: 2.13.2,2.13.3 CBI
2115574	PP450: Physico-Chemical Data File, DACO: 2.14.1,2.14.10,2.14.11,2.14.12,2.14.13,2.14.2,2.14.8,2.14.9 CBI
2115575	Statement of Odor of Flutriafol Technical Wet Paste, DACO: 2.14.3 CBI
2115576	Flutriafol pure: Melting temperature and boiling temperature, DACO: 2.14.4,2.14.5 CBI
2115577	Determination of the relative density at 20C of Flutriafiol Technical (Wet paste), Batch No. 1584/1, DACO: 2.14.6 CBI
2115578	Determination of the Water Solubility of Flutriafol Purified Active Substance, DACO: 2.14.7 CBI
2115579	Determination of the Long Term Storage Stability of Flutriafol Technical (Wet Paste) in Commercial Packaging., DACO: 2.14.14 CBI
2115580	Determination of storage stability for 14 days at 54C of Flutriafol technical (wet paste)., DACO: 2.14.14 CBI
2115581	Determination of storage stability for 14 days at 54C of Flutriafol technical (wet paste)., DACO: 2.14.14 CBI
2115682	2011, Part 2, DACO: 2.0 CBI
2115683	Letter of Name change, DACO: 2.2 CBI
2115684	[CBI removed] MSDS, DACO: 2.11.2 CBI
2115685	2007, [CBI removed], DACO: 2.11.2 CBI
2115686	2010, [CBI removed], DACO: 2.11.2 CBI
2115688	2011, [CBI removed], DACO: 2.11.2 CBI
2115689	2011, [CBI removed], DACO: 2.11.2 CBI
2115691	2011, [CBI removed], DACO: 2.11.2 CBI
2115692	2002, [CBI removed], DACO: 2.11.2 CBI
2115693	2011, [CBI removed], DACO: 2.11.2 CBI
2115694	Flow Sheet - Technical, DACO: 2.11.3 CBI
2115695	Discussion of Formation of Impurities, DACO: 2.11.4 CBI
2275878	2011-4913 Response to PMRA Deficiencies DACO 2, DACO: 2.0 CBI
2275879	2011-4913 Response to PMRA Deficiencies DACO 2, DACO: 2.0 CBI
2275883	GLP Study No. VAL 105-01 Amendment No. 2., DACO: 2.13.1 CBI
2294420	QC data on Flutriafol technical from Calachem 1 H 2012, DACO: 2.13 CBI

2115621	Independent Laboratory Validation - Analytical Method for Flutriafol in Soil (Based Upon EPA Ecological Effects Test Guidelines OPPTS 850.7100, Data Reporting for Environmental Chemistry Methods)., DACO: 8.2.2.1,8.2.2.2,8.2.2.4
2115622	Amended Report: Analytical Method Verification for the Determination of Flutriafol in Freshwater and Saltwater., DACO: 8.2.2.3
2115623	Development and Validation of the Residue Analytical Method for Flutriafol in Drinking, Ground and Surface Water., DACO: 8.2.2.3
2276286	Independent Laboratory Validation of a Flutriafol Analytical Method for Groundwater Described in Appendix 1 of SGS Institut Fresenius GmbH Report for Study No. IF-04/00159540 Entitled "Validation of Analytical Methods to Determine Flutriafol in Soil Water
2276287	Validation of Analytical Methods to Determine Flutriafol in Soil Water, Groundwater and Soil and Investigations on the Stability and the Adsorption Situation Under Sampling Conditions. , DACO: 8.2.2
2115879	Part 3, DACO: 3.1,3.1.1,3.1.2,3.1.3,3.1.4,3.2,3.2.1,3.2.2,3.2.3,3.3.1,3.3.2,3.4,3.4.1,3.4.2,3.5,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.8,3.5.9,3.6 CBI
2115880	MSDS - Flutriafol Technical, DACO: 3.2.1 CBI
2115881	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115882	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115883	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115884	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115885	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115886	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115887	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115888	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115889	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115890	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115893	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115895	MSDS - [CBI removed], DACO: 3.2.1 CBI
2115897	Analytical method VAM 083-02.Determination of Flutriafol (CAS No. 76674-21-0) in Flutriafol technical and SC formulations., DACO: 3.4.1 CBI
2115898	Validation of analytical method VAM 083-02 for determination of Flutriafol (CAS No. 76674-21-0) in Flutriafol technical and flutriafol SC formulations Study No.: VAL 083-02, DACO: 3.4.1 CBI

2115899 Determination of storage stability for 14 days at 54 C of Flutriafol 125 g/l SC formulation, lot 1FB011203 in commercial packaging., DACO: 3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.7 CBI

2115900 Determination of the density at 20 C of Flutriafol 125 g/l SC formulation, batch No. 1FB011203., DACO: 3.5.6 CBI

2115901 Determination of pH in undiluted formulation before and after storage for 14 days at 54 C of Flutriafol 125 g/l SC formulation, lot 1FB011203 in commercial packaging., DACO: 3.5.7 CBI

2115902 Physico-chemical properties of the formulation Flutriafol 125 g/l SC before and after accelerated storage at 54 C for 2 weeks., DACO: 3.5.9 CBI

2115903 Determination of long term storage stability of Flutriafol 125 g/l SC formulation, lot 1FB011203 in commercial packaging., DACO: 3.5.10,3.5.14 CBI

2115904 Flash Point., DACO: 3.5.11 CBI

2115906 Explosive properties., DACO: 3.5.12 CBI

2276402 2011-4914 Response to PMRA Deficiency DACO 3, DACO: 3.0 CBI

2276403 2011-4914 Response to PMRA Deficiency DACO 3, DACO: 3.0 CBI

2.0 Human and Animal Health

2115964 Flutriafol: Acute Oral Toxicity to the Rat of a 125 g/l SC Formulation., DACO: 4.6.1

2115965 Flutriafol: Acute Dermal Toxicity to the Rat of 125 g/l SC Formulation., DACO: 4.6.2

2115966 Flutriafol 125 g/l SC Formulation: Acute Dermal Toxicity Study in Rats., DACO: 4.6.2

2115967 Flutriafol 125 g/l SC: Acute Inhalation (Nose Only) Study in the Rat., DACO: 4.6.3

2115968 Flutriafol: Eye Irritation to the Rabbit of a 125 g/l SC Formulation., DACO: 4.6.4

2115969 Flutriafol: Skin Irritation to the Rabbit of A 125 g/l SC Formulation., DACO: 4.6.5

2115971 Flutriafol: Skin Sensitization to the Guinea Pig of a 125 g/l SC Formulation., DACO: 4.6.6

2407341 2004, Flutriafol 125 g/l SC: Local lymph node assay (LLNA) in mice (identification of contact allergen), DACO: 4.6.6

2115446 Flutriafol: 2 Year Feeding Study in Rats, DACO: 4.4.1,4.4.2,4.4.4

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2276286 Independent Laboratory Validation of a Flutriafol Analytical Method for Groundwater Described in Appendix 1 of SGS Institut Fresenius GmbH Report for Study No. IF-04/00159540 Entitled "Validation of Analytical Methods to Determine Flutriafol in Soil Water, Groundwater and Soil and Investigations on the Stability and the Adsorption Situation under Sampling Conditions: Final Report., DACO: 8.2.2

2276287 Validation of Analytical Methods to Determine Flutriafol in Soil Water, Groundwater and Soil and Investigations on the Stability and the Adsorption Situation Under Sampling Conditions., DACO: 8.2.2

2276310 Effects of CHA 1310-03 (Flutriafol 125 g/L SC) on the parasitoid Aphidius rhopalosiphi in the laboratory., DACO: 9.2.5,9.2.6

2276311	Effects of CHA 1310-03 (a SC formulation containing 125 g/L flutriafol) on the predatory mite Typhlodromus pyri in the laboratory - Dose response test., DACO: 9.2.5,9.2.6
2276312	Flutriafol: Investigation into the toxicity of a 125 g a.i./L SC formulation to the cereal aphid parasitoid Aphidius rhopalosiphi., DACO: 9.2.5,9.2.6
2276314	Flutriafol: Investigation into the toxicity of a 125 g a.i./L SC formulation to the larvae of the hoverfly *Episyrphus balteatus* (Diptera: Syrphidae)., DACO: 9.2.5,9.2.6
2276315	Flutriafol: A laboratory investigation of the toxicity to two beneficial arthropods, a ground beetle, Pterostichus cupreus (Carabidae) and a wolf spider Pardosa spp (Lycosidae)., DACO: 9.2.5,9.2.6
2276316	Effects of Flutriafol on the development of sediment-dwelling larvae of *Chironomus Riparius* in a water-sediment system, DACO: 9.3.4
2276317	Flutriafol: An early life-stage toxicity test with the fathead minnow (Pimephales promelas)., DACO: 9.5.3.1
2276319	Cheminovas Report on Attempts to Perform the Acute Oral Toxicity Study with Passerine Birds on Flutriafol., DACO: 9.6.2
2276320	Cheminovas Report on Attempts to Perform the Acute Oral Toxicity Study with Passerine Birds on Flutriafol., DACO: 9.6.2
2276321	Toxicity of flutriafol technical to Scenedesmus subspicatus in a 72-hour Algal growth inhibition test., DACO: 9.8.2
2276666	Flutriafol: toxicity to the earthworm Eisenia foetida of a 125 g litre-1 SC Formulation, DACO: 9.8.2
2276667	Flutriafol 125 g/L SC: A 96-hour toxicity test with the freshwater diatom (Navicula pelliculosa)., DACO: 9.8.2
2276668	Flutriafol: toxicity to the green alga (Selenastrum capricornutum) of a 125 g/L SC formulation., DACO: 9.8.2
2276669	Flutriafol 125 g/L SC: To determine the effects on reproduction and growth of the earthworm, Eisenia fetida., DACO: 9.9
2276672	Flutriafol: effect on earthworm population after 10 annual applications., DACO: 9.9
2276673	Flutriafol: an investigation of the effects on earthworms (Lumbricidae) of repeated annual field applications., DACO: 9.9
2276674	Flutriafol: The 28 day LC50 to rainbow trout (Oncorhynchus mykiss) of a 125 g/L SC formulation. Report number: BL5242/B., DACO: 9.9
2288386	Flutriafol 125 g/L SC: A 96-hour toxicity test with the freshwater diatom (Navicula pelliculosa)/2006, DACO: 9.8.2

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2116117	Part 10 - Flutriafol 125 SC, DACO: 10.1,10.2.1,10.2.2,10.2.3.1,10.2.3.3(D),10.3.1,10.3.2
2116119	2011, Value Summary - Canada, DACO: 10.1,10.3.1
2116122	2011, Efficacy and selectivity of TOPGUARD when foliar applied to apple for control of powdery mildew and apple scab in 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116123	2011, Efficacy and selectivity of TOPGUARD when foliar applied to apple for control of powdery mildew and apple scab in 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116125	2011, Efficacy and selectivity of TOPGUARD when foliar applied to apple for control powdery mildew in 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116128	2011, Efficacy and selectivity of TOPGUARD when foliar applied to apple for control powdery mildew in 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116129	2011, Efficacy and selectivity of TOPGUARD when foliar applied to grape for control of powdery mildew in grapes 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116130	2011, Efficacy and selectivity of TOPGUARD when foliar applied to grape for controlof powdery mildew in grapes 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116132	2011, Efficacy and selectivity of TOPGUARD when foliar applied to grape for control of powdery mildew control in grapes., DACO: 10.2.3.3(D),10.3.2(B)
2116133	2011, Efficacy and selectivity of TOPGUARD when foliar applied to grape for control of powdery mildew control in grapes 2010., DACO: 10.2.3.3(D),10.3.2(B)
2116138	2011, Efficacy and selectivity of TOPGUARD when foliar applied to strawberry for control of powdery mildew in 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116139	2011, Efficacy and selectivity of TOPGUARD when foliar applied to strawberry for control of powdery mildew in 2010, DACO: 10.2.3.3(D),10.3.2(B)
2116144	2011, Value Summary - Europe and US, DACO: 10.1,10.3.1
2196852	Crop: Strawberry (FRASS) Pest: Powdery Mildew (SPHRS) - 2004, DACO: 10.2.3.3(D)
2196853	Crop: Strawberry (FRASS) Pest: Powdery Mildew (SPHRS) - 2004, DACO: 10.2.3.3(D)
2196854	Crop: Strawberry (FRASS) Pest: Powdery Mildew (SPHRS), DACO: 10.2.3.3(D)

2196873 Crop: Soybeans (GLXMA) Pest: Phakopsora pachyrhizi - 2007, DACO: 10.2.3.3(D)

2196874 Crop: Soybeans (GLXMA) Pest: Cercospora sojina - 2009, DACO: 10.2.3.3(D)

2196876 Crop: Soybeans (GLXMA) Pest: Cercospora sojina - 2009, DACO: 10.2.3.3(D)

2196878 Crop: Soybeans (GLXMA) Pest: Phakopsora pachyrhizi - 2007, DACO: 10.2.3.3(D)

2196884 Crop: Soybeans (GLXMA) Pest: Cercospora sojina - 2007, DACO: 10.2.3.3(D)

2196886 Crop: Soybeans (GLXMA) Pest: Cercospora sojina - 2007, DACO: 10.2.3.3(D)

2196888 Crop: Soybeans (GLXMA) Pest: septoria brownspot - 2006, DACO: 10.2.3.3(D)

2196892 Crop: Soybeans (GLXMA) Pest: brown spot and frog eye - 2006, DACO: 10.2.3.3(D)

2196893 Crop: Soybeans (GLXMA) Pest: brown spot and frog eye - 2006, DACO: 10.2.3.3(D)

2196894 Crop: Soybeans (GLXMA) Pest: frog eye - 2005, DACO: 10.2.3.3(D)

2196896 Crop: Soybeans (GLXMA) Pest: frog eye - 2005, DACO: 10.2.3.3(D)

2197015 Crop: Apples (MABSD) Pest: Apple scab Venturia inequalius - 2004, DACO: 10.2.3.3(D)

2197023 Crop: Apples (MABSD) Pest: Apple powdery mildew - 2006, DACO: 10.2.3.3(D)

2197025 Crop: Apples (MABSD) Pest: Apple powdery mildew - 2006, DACO: 10.2.3.3(D)

2197027 Crop: Apples (MABSD) Pest: Apple powdery mildew - 2007, DACO: 10.2.3.3(D)

2197030 Crop: Apples (MABSD) Pest: Apple powdery mildew - 2007, DACO: 10.2.3.3(D)

2197032 Crop: Apples (MABSD) Pest: Apple powdery mildew - 2008, DACO: 10.2.3.3(D)

2197034 Crop: Apples (MABSD) Pest: Apple powdery mildew - 2008, DACO: 10.2.3.3(D)

2197035 Crop: Apples (MABSD) Pest: Apple powdery mildew, apple scab, fruit russet - 2008, DACO: 10.2.3.3(D)

2197039 Crop: Apples (MABSD) Pest: powdery mildew - 2004, DACO: 10.2.3.3(D)

2197041	Crop: Apples (MABSD) Pest: powdery mildew - 2005, DACO: 10.2.3.3(D)
2197043	Crop: Apples (MABSD) Pest: apple scab (Venturia inequalis) - 2005, DACO: 10.2.3.3(D)
2197046	Crop: Apples (MABSD) Pest: apple scab (Venturia inequalis) - 2005, DACO: 10.2.3.3(D)
2197048	Crop: Apples (MABSD) Pest: apple scab (Venturia inequalis) - 2002, DACO: 10.2.3.3(D)
2197056	Crop: Apples (MABSD) Pest: apple scab (Venturia inequalis) - 2005, DACO: 10.2.3.3(D)
2199032	Disease management by experimental fungicides on Golden Delicious, Idared, and York Imperial apples, 2009., DACO: 10.2.3.3(D)
2199033	Control of powdery mildew and other diseases by experimental fungicides and mixed schedules on Idared apples, 2010., DACO: 10.2.3.3(D)
2199034	Evaluation of experimental fungicides and mixed schedules on Stayman, Idared, and Granny Smith apples, 2010., DACO: 10.2.3.3(D)
2199035	2012, Control of apple diseases with Inspire Super, Topguard, and Fontelis, 2011., DACO: 10.2.3.3(D)
2199036	2011, M.9 block fungicide trial, 2011, DACO: 10.2.3.3(D)
2199037	2011, ASSESS THE EFFICACY & SELECTIVITY OF TOPGUARD SC WHEN FOLIAR APPLIED TO SOYBEAN, DACO: 10.2.3.3(D)
2199038	2009, Cercospora Leaf Blight ratings Multiple Fungicides 2009., DACO: 10.2.3.3(D)
2199039	Cercospora Leaf Spot 2010., DACO: 10.2.3.3(D)
2199040	2009, Efficacy and selectivity of Topguard SC for control of Soybean Rust, DACO: 10.2.3.3(D)
2199044	2009, Dean Lee ASR Fungicide Trial, DACO: 10.2.3.3(D)
2200652	Management of powdery mildew and other diseases by experimental fungicides and mixed schedules on Idared apples, 2011., DACO: 10.2.3.3(D)

B. Additional Information Considered

i) Published Information

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

4.0 Value

ii) Unpublished Information

1.0 Chemistry

2.0 Human and Animal Health

3.0 Environment

1311104 2004, Environment Canada, Unpublished Water Monitoring Data Collected In Bc; Pesticide Science Fund, DACO: 8.6

1311110 2004, Environment Canada, Presence, Levels And Relative Risks of Pririty Pesticides in Selected Canadian Aquatic Ecosystems: An Environment Canada Pesticides Science Fund Project. Year 1 (2003-04) Annual Report, DACO: 8.6

1311111 2005, Environment Canada, Unpublished Pesticide Science Fund Annual Report 2004-2005. (Water, Air, Plants, Mammals and Amphibians; And Fish And Birds). DACO: 8.6

1311112 2004, Environment Canada, Unpublished National Water Monitoring Data. Pesticide Science Fund (2004), DACO: 8.6

1403269 2006, Environment Canada, Pesticide Science Fund Annual Report 2005-2006, DACO: 8.6

1971119 2010, Raw Unpublished Pesticide Science Fund Water Monitoring from Mill Creek British Columbia, DACO: 8.6

2210920 2006, EFSA, Flutriafol - Volume 3, Annex B.8 - Environmental Fate and Behaviour, DACO: 12.5.8

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